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(54) Title: SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR INTEGRATING BIOLOGICAL/CHEMICAL DATABASES TO CREATE AN ONTOLOGY NETWORK

(57) Abstract: Biological/chemical databases are integrated by obtaining an entity-relationship model for each of the biological/chemical databases, and identifying related entities in the entity-relationship models of at least two of the biological/chemical databases. At least two of the related entities that are identified are linked, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases. The entity-relationship model that integrates the biological/chemical databases provides an ontology network that integrates the diverse ontologies that are represented by the independent biological/chemical databases. By navigating the entity-relationship model in response to queries, discovery may be obtained that may not be obtainable from any one of the independent biological/chemical databases.

SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR INTEGRATING BIOLOGICAL/CHEMICAL DATABASES TO CREATE AN ONTOLOGY NETWORK

Cross Reference to Provisional Applications

This application is related to and claims the benefit of U.S. Application Serial No. _____ to Wilbanks, Levy, Segaran and Gardner, filed May 13, 2002, entitled *Systems, Methods and Computer Program Products for Integrating Biological/Chemical Databases to Create an Ontology Network* (Attorney Docket 9223-10), which itself is related to and claims the benefit of Provisional Application Serial No. 60/296,018 to Levy and Segaran, filed June 5, 2001, entitled *Cell: A Cross-Referenced Ontological Database for Biological Data*; and Provisional Application Serial No. 60/356,616 to Gardner and Wilbanks, filed February 13, 2002, entitled *Ontology Networks, a New Foundation for Discovery*, all of which are assigned to the assignee of the present application, the disclosures of all of which are hereby incorporated herein by reference in their entirety as if set forth fully herein.

Field of the Invention

This invention relates to bioinformatics/cheminformatics, and more particularly to systems, methods and computer program products for processing biological databases and/or chemical databases.

Background of the Invention

The biotechnology, chemical and pharmaceutical industries continue to attempt to develop innovative and effective drugs, chemicals, agricultural and/or other products on shorter schedules and at reduced cost. A potential challenge faced in this pursuit is managing the enormous volume, diversity and complexity of data that is currently being generated by these industries. In particular, new technologies have resulted in an enormous increase in the amount of data available to researchers. Unfortunately, this enormous increase in the amount of data may not lead to

corresponding advances in discovery, because the sheer volume of data may outpace the ability of researchers to transform that data into knowledge.

In an attempt to analyze these massive amounts of data, the field of bioinformatics has emerged. See, for example, U.S. Patent Application Serial No. 09/657,218 to Wilbanks et al., filed September 7, 2000, entitled *Systems, Methods and Computer Program Products for Processing Genomic Data In An Object Oriented Environment*, assigned to the assignee of the present application, the disclosure of which is hereby incorporated herein by reference in its entirety as if set forth fully herein.

The massive volume of data that is being generated also may be accompanied by a large diversity of data sources that may generate the data. For example, public, private, proprietary, clinical, chemical, genomic and other databases from various data sources may be produced. Unfortunately, it may be difficult to integrate these heterogeneous data sources.

One conventional approach for data integration uses a data warehouse and data mining techniques. A data warehouse may use a relational database and a star model in which searchable database fields are stored in their own tables, forming a star around a table of records. Unfortunately, it may be difficult to integrate new types of data without significant modification to the table structure. Moreover, querying the assembled information using conventional data mining techniques also may present potential problems. These queries may range in sophistication from simple use of Boolean operators, data search engines such as Internet-based search tools, and/or more sophisticated query languages that employ relational inquiries into the database. Unfortunately, these queries may require significant knowledge of the data sources, the structure of the assembled data, and/or experience in the use of query languages. The use of Internet-based search engines may yield inaccurate yet exhaustive reams of information that may not be relevant to the original request.

Another conventional approach that may be used for data integration is the flat-file or link-driven federation, wherein users can perform text searching on the databases independently, and then jump to different databases, for example via World Wide Web links. Although a flat-file or link-driven federation may simplify searching for non-expert users, it may be difficult to search across multiple databases simultaneously. Moreover, it may be difficult to obtain desired information for data records that only are indirectly and/or inferentially linked.

Another conventional integration technique is referred to as a wrapper or view, which can provide cross-database querying without moving data from the original databases. For each database, a separate driver may be designed that can query the database. A wrapper can then ask several databases for some results and bring them together to find intersections. Unfortunately, it may be difficult to bring in new data types, as new drivers may need to be provided for every new data source. Moreover, queries may be slow and memory-intensive, because all relevant databases may need to be queried for their entire result set before elimination by any other parts of the query is performed. Finally, relationships may not be provided unless specified in the queries and/or wrappers.

Summary of the Invention

Some embodiments of the present invention integrate a plurality of biological/chemical databases by obtaining an entity-relationship model for each of the plurality of biological/chemical databases, and identifying related entities, including identical entities, in the entity-relationship models of at least two of the biological/chemical databases. At least two of the related entities that are identified are linked, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases. In some embodiments, when the entities are identical entities, they are merged. In some embodiments, each of the plurality of databases represents an ontology and the entity-relationship model that integrates the plurality of biological/chemical databases creates an ontology network.

Accordingly, ontology networks according to some embodiments of the present invention can link related entities in entity-relationship models of independent biological/chemical databases, to thereby create a single entity-relationship model for the independent biological/chemical databases. By navigating the single entity-relationship model in response to queries, discovery may be obtained that may not be obtainable from any one of the independent biological/chemical databases.

In some embodiments, linking is performed by merging at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases. In other embodiments, merging is accomplished by establishing a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical

databases, a respective alias of which refers to a respective one of the identical entities that are identified.

In some embodiments, the traversing is performed from a starting entity to an ending entity in response to a query that specifies the starting entity and the ending entity. In other embodiments, the entities are traversed from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity. In yet other embodiments, the entities are traversed in response to a query and in response to at least one path rule. In some embodiments, the at least one path rule specifies the type of path to use in traversing through the plurality of entities, the type of path not to use in traversing through the plurality of entities, the type of ending entity that can be included in the query results, the type of ending entity that is not to be included in the query results, the type of relationship to be used in traversing through the plurality of entities, the type of relationship that is not to be used in traversing through the plurality of entities and/or a confidence level to be achieved in traversing through the plurality of entities. In still other embodiments, groups of relationships may be classified into a class of relationships, and the at least one path rule can specify a class of relationships to be included or excluded. Multiple classes can be assigned to a given relationship.

In other embodiments, the query results are stored as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases, to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases. In still other embodiments, a confidence level is assigned to at least one of the relationships in the entity-relationship model that integrates the plurality of biological/chemical databases. In still other embodiments, query results also may be based on assigned confidence levels.

According to other embodiments of the present invention, a new biological/chemical database may be integrated with a plurality of biological/chemical databases, by providing an entity-relationship model of the plurality of biological/chemical database that links at least some related entities in at least two of the biological/chemical databases. An entity-relationship model for the new biological/chemical database is obtained. Related entities in the entity-relationship model of the new biological/chemical database and the entity-relationship model of the plurality of biological/chemical databases are identified. At least two of the

related entities that are identified are linked, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database. In other embodiments, the entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in the at least two of the biological/chemical databases provides an ontology network and the entity-relationship model of the new biological/chemical database represents an ontology.

In other embodiments of the invention, when linking identical entities, the at least two of the identical entities that are identified are merged into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database. In other embodiments, merging may be accomplished by establishing a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database. A respective alias refers to a respective one of the at least two of the identical entities that are identified.

In other embodiments, the new biological/chemical database is an updated version of one of the plurality of biological/chemical databases. In some of these embodiments, at least one entity is identified that is in the one of the plurality of biological/chemical databases and that has been deleted from the updated version of the one of the plurality of biological/chemical databases. An alias that is associated with the at least one entity is removed. In still other embodiments, at least one entity is split based upon the alias that was removed. In yet other embodiments, an image of the at least one record that has been deleted may be retained in the plurality of biological/chemical databases, so as to allow an archival history to be maintained. In still other embodiments, multiple images or instances of the entity/relationship structure may be maintained to reflect updates and/or deleted records and/or query results, and these multiple instances may be correlated to one another to obtain new knowledge.

In still other embodiments, when adding a new biological/chemical database, entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database are identified. At least one new entity is added to the entity-relationship model that

corresponds to the entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model.

Bioinformatics data processing systems according to some embodiments of the present invention include an ontology network engine that is configured to build an integrated entity-relationship model of a plurality of independent biological/chemical databases. The entity-relationship model comprises a plurality of entities including links and also comprises a plurality of relationships. In some embodiments, a metadata database is configured to store therein the integrated entity-relationship model of the plurality of independent biological/chemical databases. In other embodiments, a loader is configured to load an independent entity-relationship model of each of the independent biological/chemical databases into the ontology network engine. The independent biological/chemical databases may be loaded in a typeless format. Other embodiments include a virtual experiment layer that is configured to conduct virtual experiments on the integrated entity-relationship model. Yet other embodiments include a discovery layer that is configured to discover biological/chemical knowledge from the integrated entity-relationship model. Moreover, in still other embodiments, the integrated entity-relationship model provides a bioinformatics data structure. Finally, it will be understood that any of the embodiments described herein may be provided as systems, methods and/or computer program products.

Brief Description of the Drawings

Figures 1 and 2 illustrate conceptual overviews of environments in which some embodiments of the present invention may be used.

Figure 3 is a hardware/software block diagram of some embodiments of the present invention.

Figure 4 is a software architecture diagram of some embodiments of the present invention.

Figure 5 is a flowchart of operations for integrating biological/chemical databases according to some embodiments of the present invention.

Figure 6 is a flowchart of operations for integrating a new biological/chemical database into a plurality of biological/chemical databases according to some embodiments of the present invention.

Figure 7 is a flowchart of operations for querying a plurality of biological/chemical databases according to some embodiments of the present invention.

Figure 8 is an example of a portion of an entity-relationship data structure that integrates multiple biological/chemical databases according to some embodiments of the present invention.

Figure 9 is a flowchart of operations for integrating biological/chemical databases according to some embodiments of the present invention.

Figure 10 is a flowchart of operations for integrating new biological/chemical databases according to some embodiments of the present invention.

Figure 11 is a flowchart of operations for performing queries according to some embodiments of the present invention.

Figures 12-17 conceptually illustrate an example of the creation of an ontology network according to some embodiments of the present invention.

Figure 18 illustrates an example of querying an ontology network that was created in Figures 12-17 according to some embodiments of the present invention.

Figure 19 illustrates another example of an ontology network that may be created according to some embodiments of the present invention.

Figure 20 is an example of linkages that may be provided by an ontology network of Figure 19 according to some embodiments of the present invention.

Figure 21 illustrates a browser display of a portion of an ontology network according to some embodiments of the present invention.

Figure 22 is a block diagram of a data processing architecture that may be used with some embodiments of the present invention.

Figures 23A and 23B, which together form Figure 23, is an entity-relationship diagram of a conceptual schema for an ontology network according to some embodiments of the present invention.

Figures 24 and 25 are flowcharts of operations for integrating biological/chemical databases and integrating new biological/chemical databases according to some embodiments of the present invention.

Figure 26 is a flowchart illustrating operations for traversing an ontology network using path rules according to some embodiments of the present invention.

Figure 27 is an example of an *in silico* experiment that can be derived from an ontology network according to some embodiments of the present invention.

Figures 28-35 illustrate an example of a path rule that may be used to obtain discovery according to some embodiments of the present invention.

Figure 36 illustrates an example of a display screen that may be used to initiate a query using a path rule that was specified in Figures 28-35 according to some embodiments of the present invention.

Figures 37A and 37B, which together form Figure 37, illustrates an example of a display screen of query results that may be obtained according to some embodiments of the present invention.

Figures 38 and 39 are flowcharts of operations for querying an ontology network according to some embodiments of the present invention.

Figure 40 illustrates a conceptual overview of environments in which some embodiments of the present invention may be used.

Figures 41 and 42 illustrate examples of ontology networks that can be used to link personal data, securities data and government data according to some embodiments of the present invention.

Detailed Description of Preferred Embodiments

The present invention now will be described more fully hereinafter with reference to the accompanying figures, in which embodiments of the invention are shown. This invention may, however, be embodied in many alternate forms and should not be construed as limited to the embodiments set forth herein.

Accordingly, while the invention is susceptible to various modifications and alternative forms, specific embodiments thereof are shown by way of example in the drawings and will herein be described in detail. It should be understood, however, that there is no intent to limit the invention to the particular forms disclosed, but on the contrary, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the claims. Like numbers refer to like elements throughout the description of the figures.

The present invention is described below with reference to block diagrams and/or flowchart illustrations of methods, apparatus (systems) and/or computer program products according to embodiments of the invention. It is understood that each block of the block diagrams and/or flowchart illustrations, and combinations of blocks in the block diagrams and/or flowchart illustrations, can be implemented by computer program instructions. These computer program instructions may be

provided to a processor of a general purpose computer, special purpose computer, and/or other programmable data processing apparatus to produce a machine, such that the instructions, which execute via the processor of the computer and/or other programmable data processing apparatus, create means for implementing the functions/acts specified in the block diagrams and/or flowchart block or blocks.

These computer program instructions may also be stored in a computer-readable memory that can direct a computer or other programmable data processing apparatus to function in a particular manner, such that the instructions stored in the computer-readable memory produce an article of manufacture including instructions which implement the function/act specified in the block diagrams and/or flowchart block or blocks.

The computer program instructions may also be loaded onto a computer or other programmable data processing apparatus to cause a series of operational steps to be performed on the computer or other programmable apparatus to produce a computer-implemented process such that the instructions which execute on the computer or other programmable apparatus provide steps for implementing the functions/acts specified in the block diagrams and/or flowchart block or blocks.

It should also be noted that in some alternate implementations, the functions/acts noted in the blocks may occur out of the order noted in the flowcharts. For example, two blocks shown in succession may in fact be executed substantially concurrently or the blocks may sometimes be executed in the reverse order, depending upon the functionality/acts involved.

Definitions

As used herein, the following terms have the following meanings:

Biological/chemical: Biological and/or chemical.

Biological database: A database that includes, at least in part, data describing or related to biological experiments and/or concepts at any number of biological levels, from population to organism to gene and/or protein sequence. Examples include, but are not limited to, the well known KEGG, MaizeDB, OmIm and HGMD databases. Biological databases can include genomic databases that include, at least in part, data containing genome sequence and/or data related to genome sequence such as annotation and/or gene prediction. Examples of genomic databases include, but are not limited to, the well known ENSEMBL, WormPep and Celera Human

Genome databases. Biological databases can also include proteomic databases that include, at least in part, data from or related to proteomic experiments, such as 2d-gel, or results from high-throughput mass spectrometry. Examples of proteomic databases include, but are not limited to, the well known Swiss-2D-PAGE database. Biological databases also can include classification databases, examples of which include, but are not limited to, the well known MeSH, Gene Ontology Consortium (GO) and Enzyme databases. Biological databases also can include sequence databases that include, at least in part, data containing biomolecule sequence information, such as nucleotide, peptide and/or carbohydrate sequence and/or annotation. Examples of sequence databases include, but are not limited to, the well known GenBank and SWISS-PROT databases. Biological databases also can include toxicity, disease, clinical trial and/or other databases that describe or relate to biological experiments and/or concepts at any number of biological levels, from population to organism to gene and/or protein sequence.

Chemical database: A database that includes, at least in part, chemical information such as chemical structures, formulae, nomenclature, properties and/or biochemical action of organic and/or inorganic chemicals. Examples include, but are not limited to, the well known ChemID+ database.

Entity-relationship: A data model that views information as a set of basic objects (entities) and relationships among these entities. An entity is an object or concept about which information is stored. An entity may have attributes which are the properties or characteristics of the entity. Relationships indicate how two entities share information. Relationships may also have attributes or properties. The entity-relationship model was originally developed by Dr. Peter P. Chen and was adopted as the meta model for the American National Standards Institute (ANSI) Standard on Information Resource Directory System (IRDS). In a biological/chemical database, examples of entities include, but are not limited to, 2D-gel-spot, carbohydrate, chemical, classification, disease, express-in, gene, gene-product, interaction, keyword, literature, localization, locus, motif, nucleotide-sequence, oligonucleotide, pathway, physical location, protein, symbol, taxonomy, related-group, marker, pseudogene, strain, tissue-cell-type, variation, reaction, clone, experiment, experiment-result, structure and sequence-library, and examples of relationships include kind of, reaction type, default, path, reaction-left, reaction-right, annotation, available oligonucleotide, catalysis, enzyme classification, enzyme in pathway, expression, glycosylation,

homology, homology cluster, in species, inheritable locus, isomer, kind-of, mapping, marker, nomenclature, occurs-in, ontological, part of complex, part of experiment, part of interaction, part of pathway, part of structure, partial-sequence, protease-class, protein contains motif, pseudogene, reaction type, reference, related, result probe, same gene product, same protein, sequenced, spot contains, transcription, translation, variation, in strain, reactant, library sequence, exon-gene-annotation, exon-sequence-annotation, and mapped-between.

Ontology: A structured vocabulary of terms and some specification of their meaning and/or relationships among one another based on a set of beliefs about the terms and their meanings/relationships. The structure can be explicit and/or implicit.

Other terms used herein have their ordinary meaning to those having skill in the art, unless specified otherwise, and, therefore, need not be expressly defined herein.

Referring now to Figure 1, a conceptual overview of environments in which embodiments of the present invention may be used, is shown. As shown in Figure 1, these environments may include large amounts of data from many biological/chemical experiments **102** that may be collected in many disparate or independent databases including public, private, proprietary, clinical, chemical, genomic and/or other databases **104**. Each database may have associated therewith a quality control tool **106** that can check for errors, database integrity and/or other parameters within the individual database.

Still referring to Figure 1, data mining tools may be used as were described above, to allow searching within and/or across databases **104**. However, data mining/data warehousing may have shortcomings in integrating and/or querying diverse databases. Moreover, in other embodiments, data mining tools need not be used.

Still referring to Figure 1, some embodiments of the present invention may provide knowledge mining, using aliases and/or ontology networks, wherein a plurality of biological/chemical databases is integrated, so that new knowledge may be established by querying the integrated data structure. This knowledge mining can lead to the running of virtual experiments **112**, also referred to as *in silico* experiments, using the integrated databases and one or more virtual experiment tools. These virtual experiments **112** then can lead to new discoveries **114** which may be

obtained using one or more discovery tools. Accordingly, embodiments of the present invention can provide a knowledge mining layer **110** that can allow virtual experiments **112** and discovery **114**, respectively, to be obtained, based on independent biological/chemical databases **104** that are collected from disparate sources.

Referring now to Figure 2, another conceptual overview of environments in which embodiments of the present invention may be used is shown. As shown in Figure 2, a plurality of disparate biological/chemical databases may be provided. For example, a genomic/proteomic database **202a**, a biomolecule database **202b**, a phenotypic database **202c**, a public database **202d** and a curated/third party database **202n** may be provided. More or fewer databases also may be provided, and one or more of these databases may be merged or bifurcated.

Each of these databases **202a-202n** includes records for a plurality of biological/chemical objects, also referred to herein as entities. These databases **202a-202n** also generally include an indication of one or more relationships among the various biological/chemical objects, to thereby define an entity-relationship data structure or model for each of the independent databases. The entity-relationship data structure for each database may be thought of as defining an ontology, which provides a vocabulary of terms and some specification of their meaning and/or relationships among one another. These entities and relationships may represent a set of beliefs on the part of the database creator or other individual(s)/organization(s). Thus, the ontology in a given database **202a-202n** represents a belief system about the entities and relationships of the data in the database. Some of the databases **202a-202n** may constitute a relational database data model that does not explicitly contain entity-relationship data structures. However, entity-relationship data models may be derived from these data models using conventional techniques, in some embodiments of the invention. In other relational database models, one or more entities may be present or derivable, but relationships may not be present or implicit in the data models. According to some embodiments of the invention, these data models can be integrated with other databases that include an ontology, to provide an ontological context for the data model as well.

Referring again to Figure 2, the databases **202a-202n** may constitute a data collection layer that may be derived from, for example, wet laboratory experiments. Some of this data may be processed in a quality control layer by data analysis/quality

control modules **204a, 204b...204n**. These data analysis/quality control modules may provide some data curation and determination of clusters of meaningful information. Other databases, such as databases **202d** and **202n**, may not include an analysis/quality control layer.

Still referring to Figure 2, in some embodiments, at least some of the raw, compressed and/or qualified data may be incorporated into a warehouse by a data integration/data mining layer **206**, which can enable the organization of the data into logically structured tables of information. Data querying may conventionally be performed at the data integration/data mining tool or layer **206**, for example by developing specialized query requests to gain inference or knowledge from the warehouse. In other embodiments, a data integration/data mining tool **206** is not used.

In some environments, embodiments of the present invention may operate on top of this data integration/data mining tool **206**, and/or may also operate directly on a biological/chemical database, such as the chemical data and cheminformatics database **208**, and/or the pre-clinical database **214**. The preclinical database **214** may include ADME, toxicity, pharmaco-kinetics and/or other data. Some embodiments of the present invention can provide a knowledge mining layer in the form of an ontology network **210** that can overlay/merge/associate diverse ontologies that are represented in diverse databases, data tables and/or data repositories. The resulting ontology network **210** thus can link multiple disparate ontologies.

As will be described in more detail below, according to some embodiments of the present invention, an ontology network **210** can incorporate the entity-relationship models of the databases on which it is built, but can also define new relationships or hierarchies by the process of overlay, merge and/or association of entities from the independent ontologies. This conceptualization of knowledge can serve as a specification mechanism for the development of a broad-mesh belief system that can deliver experimental insight. Stated differently, ontology networks **210** according to some embodiments of the present invention can traverse and, thereby, establish a linked path of relationships creating associations between characteristically unlike entities, to thereby allow the revelation of new information and knowledge. The resulting lattice of semantically rich metadata can form an ontology network **210** that captures the knowledge from the data sources **202, 208** it supports.

Thus, as shown in Figure 2, in some embodiments of the present invention, an ontology network **210** can be located above the data integration layer **206**, and can

provide a knowledge tool or layer that is available for hypothesis or question-driven mining, as opposed to complex data mining queries that may be typical of data mining applications. Thus, some embodiments of the invention can provide a meta-database of entities and/or relationships that can allow efficient and intelligent analysis of accumulated data.

Still referring to Figure 2, ontology networks **210** according to some embodiments of the present invention may be linked to an application tool or layer, such as a discovery/prediction and simulation tool **212**, so as to allow more accurate discovery, prediction and/or simulation. Examples of a discovery/prediction and simulation layer **212** are described in Provisional Application Serial No. 60/346,694 to Segaran and Pan, filed January 7, 2002, entitled *Analysis of Functional Cellular Pathways and the Role of Structural Homology on Chemosensitivity*, the disclosure of which is hereby incorporated herein by reference in its entirety as if set forth fully herein.

Referring now to Figure 3, a hardware/software block diagram of some embodiments of the present invention now will be described. It will be understood that some embodiments of the present invention may execute on one or more personal, application and/or enterprise computer systems, in a standalone, networked, distributed, pervasive, peer-to-peer and/or other configuration.

Referring now to Figure 3, a data processing engine **300**, which also may be referred to as an ontology engine, can be used to integrate, update and/or query a plurality of databases, and/or generate, add to and/or query an ontology network as will be described in detail below. The engine **300** can provide a knowledge mining layer **110** of Figure 1 and/or an ontology network **210** of Figure 2 in some embodiments. The engine **300** is responsive to one or more loaders **302** that can extract relevant information from one or more biological/chemical databases **304**, which can be analogous to the data collection layer **104** of Figure 1 and/or the databases **202, 208** of Figure 2. In some embodiments, *a priori* knowledge of the semantics of the ontology that is represented by the associated biological/chemical databases **304** is built into the loader **302** of that ontology's external data files. Moreover, in some embodiments, the loader **302** has knowledge of the semantics of the appropriate part of the engine **300**, to which the ontology data connects.

In some embodiments, the engine **300** generates metadata in the form of an overlaid/merged/associated entity-relationship data structure, which can be stored in a

metadata database **308**. One or more applications **306** may be used for providing discovery, prediction, simulation and/or other applications, analogous to the discovery layer **114** of Figure 1 or the discovery/prediction and simulation layer **212** of Figure 2. These applications **306** can interface with a local user interface and/or can interface with a Web browser **316** that is connected to a Web server **312**, for example, via a network, such as the Internet **314**. The design of a Web server **312**, a network such as the Internet **314**, and a Web browser **316** is well known to those having skill in the art and need not be described further herein. Finally, user-defined path rules **322** and/or predefined path rules **324** may be provided to allow directed path traversals as will be described in detail below.

Figure 4 is a software architecture diagram of some embodiments of the present invention. These embodiments may be used on one or more personal, application and/or enterprise computer systems in a standalone, networked, distributed, pervasive, peer-to-peer and/or other configuration. As shown in Figure 4, a data processing engine **400** can generate the metadata for a metadata database **408** as will be described in detail below. An Application Programming Interface (API) **430** may be provided to interface the engine **400** with one or more external database loaders **402** and one or more applications **406**. The engine **400**, metadata database **408**, loaders **402** and applications **406** may be analogous to elements **300**, **308**, **302** and **306**, respectively, of Figure 3.

Referring now to Figure 5, operations for integrating biological/chemical databases according to some embodiments of the present invention now will be described. It will be understood that these operations may be embodied, for example, in a knowledge mining layer **110** of Figure 1, an ontology network **210** of Figure 2, an engine **300** of Figure 3 and/or an engine **400** of Figure 4. These embodiments can integrate a plurality of disparate or independent biological/chemical databases, such as the databases **202a-202n** and **208** of Figure 2, and/or **304** of Figure 3, each of which includes records for a plurality of biological/chemical objects.

Referring now to Block **502**, a set of records is identified in the plurality of biological/chemical databases that relates to (i.e., is associated with) a single biological/chemical object. At Block **504**, an entity is established in a data structure that corresponds to the single biological/chemical object. The entity includes a plurality of aliases, a respective one of which refers to a respective record in the set of records in the plurality of biological/chemical databases. At Block **506**, if there are

more records, the operations for identifying and establishing (Blocks **502** and **504**, respectively), are repeatedly performed for a plurality of sets of records and, in some embodiments, for all sets of records, in the plurality of biological/chemical databases, to establish a plurality of entities in the data structure.

Still referring to Figure 5, in other embodiments of the invention, as shown at Block **510**, the plurality of entities in the data structure are linked in an entity-relationship model of the plurality of biological/chemical databases. It will be understood that the operations of Block **510** may be performed in parallel with the operations of Block **504**, and need not be performed after a plurality or all sets of records have been identified (Block **502**) and entities have been established (Block **504**).

Still referring to Figure 5, according to other embodiments of the invention, at Block **512**, a query may be received. The query may be received from an application or other program with or without direct user intervention. As shown at Block **514**, the query may identify or specify a path type through the entity-relationship model. As shown at Block **516**, in some embodiments, if no path type is identified, the plurality of entities that are linked in an entity-relationship model is traversed in response to a query, to thereby obtain query results that are based on the records in the plurality of biological/chemical databases. In contrast, at Block **518**, if a path type is identified, the plurality of entities that are linked in an entity-relationship model is traversed along the identified type of path or paths in response to a query, to thereby obtain query results that are based on the records in the plurality of biological/chemical databases. These query results may be provided at Block **520** via an application, such as an application tool **306** of Figure 3 and/or **406** of Figure 4. These queries may provide virtual experiments and/or discovery (Blocks **112** and **114** of Figure 1), and/or discovery/prediction and simulation (Block **212** of Figure 2). These queries also may represent discovery processes that are recorded and reused.

As will be described in detail below, in some embodiments, the query may specify a starting entity and an ending entity, and the operations of Block **516** can traverse the plurality of entities that are linked in the entity-relationship model from the starting entity to the ending entity, to thereby identify relationships between the starting entity and the ending entity that are based on the entity-relationship model of the plurality of biological/chemical databases. In other embodiments, the entities are traversed from a starting entity to a plurality of ending entities in response to a query

that specifies the starting entity, to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the entity-relationship model of the plurality of biological/chemical databases.

Moreover, the path type of Block **514** may be identified using one or more path rules, such as user-defined path rules **322** and/or predefined path rules **324** of Figure 3. The path rules may specify, for example, a type of path to use in traversing through the plurality of entities, a type of path not to use in traversing through the plurality of entities, a type of ending entity that can be included in the query results, a type of ending entity that is not to be included in the query results, a type of relationship to be used in traversing through the plurality of entities, a type of relationship that is not to be used in traversing through the plurality of entities and/or a confidence level to be achieved in traversing through the plurality of entities. Many other path rules also may be provided.

Finally, when the query results are provided in the Block **520**, some embodiments store the query results that are based on the entity-relationship model of the plurality of biological/chemical database, as at least one new relationship is the entity-relationship model. Knowledge that was derived from the query thereby may be stored in the entity-relationship model.

Referring now to Figure 6, operations for integrating a new biological/chemical database into a plurality of biological/chemical databases, each of which includes records for a plurality of biological/chemical objects, according to some embodiments of the present invention, now will be described. At Block **602**, a data structure is provided that includes a plurality of entities, a respective one of which corresponds to a single biological/chemical object. At least some of the entities include a plurality of aliases, a respective one of which refers to a record in a respective one of the plurality of biological/chemical databases that relates to a single biological/chemical object. In some embodiments, the operations of Block **602** may be provided by performing the operations of Blocks **502-510** in Figure 5. Thus, a preexisting data structure may be provided, and/or a data structure may be generated as was described in Figure 5.

Referring again to Figure 6, at Block **604**, records are identified in the new biological/chemical database that correspond to at least one of the entities in the existing data structure. In some embodiments, the new biological/chemical database includes an entity-relationship model or an entity-relationship model is generated

therefor. In other embodiments, the new database may merely be a relational database data model that does not, explicitly or implicitly, define relationships. By integrating the entity or entities in this new database with the existing entity-relationship model, an ontological context can be provided for the new database. Then, at Block **606**, aliases are added to at least one of the entities of the data structure that correspond to the records in the new biological/chemical database, to thereby integrate the new biological/chemical database into the plurality of biological/chemical databases. Thus, additional biological/chemical databases may be readily integrated into the data structure for a plurality of biological/chemical databases.

Referring again to Figure 6, in other embodiments of the invention, operations may be provided for identifying when a record in the new biological/chemical database corresponds to two or more entities in the existing data structure (Block **608**). If this is the case, then at Block **610**, the two or more entities in the existing data structure are merged into a new entity that includes aliases that correspond to the records associated with the two or more entities in the data structure, as well as the record in the new biological/chemical database that corresponds to the two or more entities in the data structure. Thus, the data structure can be modified as new databases are incorporated.

Still referring to Figure 6, operations may be performed according to other embodiments of the present invention, when the new biological/chemical database is an updated version of one of the plurality of biological/chemical databases that already are contained in the data structure. Thus, as shown at Block **612**, at least one record in the one of the plurality of biological/chemical databases that has been deleted from the updated version of the one of the plurality of biological/chemical databases is identified. At Block **614**, when such a record has been identified, the at least one record is removed from the one of the plurality of biological/chemical databases that has been deleted. At Block **616**, aliases that are associated with the at least one record also are removed. Moreover, at Block **618**, the at least one entity in the data structure may be split based upon the aliases that were removed. Thus, as new versions of one or more of the databases are incorporated to replace an older version, the data structure may be updated.

In yet other embodiments of the invention, when the data structure is updated by addition, deletion and/or splitting, an image, instance or version of the earlier data

structure may be maintained. This image may be used for archival purposes, to ascertain the state of the data structure during a discovery, according to some embodiments of the invention. In other embodiments, comparisons may be made between different images of the data structure, to itself lead to new discovery. Thus, for example, one image of the entity-relationship model can store data related to successful drug discoveries, from genomic to clinical indicators, to extract traversal patterns related to likelihood of success. Another image can store a similar set of patterns for expensive drug failures that did not make it through a genomic, pre-clinical or clinical phase. These images can be compared in order to obtain discovery that can predict success.

Referring now to Figure 7, operations for querying a plurality of biological/chemical databases, each of which includes records for a plurality of biological/chemical objects, now will be described according to some embodiments of the present invention. As shown in Figure 7 at Block **602**, a data structure including a plurality of entities and a plurality of aliases, is provided, as already was described in connection with Figure 6. Then, the plurality of entities that are linked in an entity-relationship model is traversed in response to a query, to thereby obtain query results, for example using operations **512-520** of Figure 5. These operations will not be described again for the sake of brevity.

Additional qualitative discussion of integration and/or querying of biological/chemical databases according to some embodiments of the present invention that were described in Figures 5-7 now will be provided. In particular, some embodiments of the invention can import different types of experimental, sequence, chemical, annotation, or other data from a Tab-Separated-Value (TSV) format, a simple eXtensible Markup Language (XML) format and/or other formats. Scripts may be provided to convert all common data formats to this TSV, XML and/or other formats. Some embodiments can create biological entities with many different aliases, parents and children. Entities can be merged if they are found to be equivalent. The entities may be organized in Directed Weighted Graph (DWG) based ontologies, as well as hierarchical and/or single level classifications. For non-expert users, a HyperText Markup Language (HTML)-based database viewer, which allows the user to search for terms and then move between different entities via hyperlinks, may be provided. Other embodiments also can produce a tool for traversing across multiple relationships to construct a logical path. Yet other embodiments can provide

a tool for importing stored traversals in order to automatically execute those traversals across multiple entities.

Thus, some embodiments of the invention can provide a cross-reference query tool for searching across multiple databases, returning only entities which meet the specified query criteria in all databases. Other embodiments also can provide a translation and annotation tool that can allow translation from one naming system to another naming system, and automatic annotation of data files using different naming systems with description data from differing imported databases. Still other embodiments can provide a clustering engine and viewer, which can allow a user to take clustered experimental data from another program and compare it with data clustered by differing data types (e.g., molecular function) to see how well the experimental clusters predict the annotation clusters and if there are additional annotation clusters. Finally, still other embodiments can provide an unsupervised grouping search, which can take a list of clustered biological entities (e.g., genes showing a similar expression pattern) and can automatically generate a hypothesis of why they are grouped.

Accordingly, some embodiments of the present invention can bridge the naming system barrier by acquiring information from databases with names of entities residing in multiple repositories, and merging one or many entities as appropriate. Heretofore, lack of merging may have been a barrier to query expansion. In particular, biological research often includes the understanding that a natural and intuitive relationship exists between components of biological entities, such as a cell, cell walls, genes, proteins, sequences, etc., and these relationships can be documented to provide a mechanism to build a traversal across multiple such entities, to establish an interpreted or inferred solution. These traversals also can identify a cause and effect relationship. Embodiments of the invention can merge the different names of the identical entities from different unintegrated (independent) data repositories, to thereby allow these traversals to be accomplished. Thus, embodiments of the present invention can apply an integration layer above the disparate data repositories and, therefore, can bind many related data repositories together. These embodiments can enable and promote increased biological context and information mining.

Some embodiments of the invention can generate, expand, update and/or query a data structure containing many nodes, each representing a biological entity (such as a protein, a gene, a protein family, or a literature reference) with multiple

aliases. Using biological entity nodes, rather than a different table for each database (as in a star schema), means that all records in diverse biological/chemical databases that represent the same object can be merged into a single entity. For example, many "integrated" databases, include a table of SWISS-PROT records and a table of PIR records, which would be joined by a reference point or hub. A cross-reference in the SWISS-PROT entry may indicate that it is the same protein as a PIR entry. In contrast, in some embodiments of the invention, these records are used to create a single biological entity, label it with a category "protein" and establish aliases from both SWISS-PROT and PIR so it can be referenced using either naming system.

In other embodiments, the entities or nodes are connected by relationships into a DWG, which means that every entity can have multiple children and multiple parents. Because there are so many categorization methods for biological entities such as genes and proteins, there may be a need for multiple non-identical groupings for an entity. The DWG allows a single entity to be grouped with other entities by as many different methods as desired, while still allowing these groups to be kept separate from each other.

In other embodiments, the data structure is also designed to be typeless, meaning that, although each entity is associated with a specific category, the same data structure can be used to represent all entities, as well as relationships between them. By using the same data structure, the data structure can potentially store any type of data without any modification. Moreover, some embodiments of the present invention can traverse the DWG unsupervised, so that these embodiments do not need to be told which path to take in order to find relationships or similarities.

Some embodiments of the invention may be implemented in both object oriented and Relational Database Management Systems (RDBMS) models, each of which may have potential advantages. One of the potential advantages of a relational database is that it may be queried with Structured Query Language (SQL). Also, since potential users may already own an RDBMS, deployment can be simpler. If a user does not own an RDBMS there are many systems available. A potential advantage of an object oriented database implementation is that interaction with object-oriented software can be simpler than with an RDBMS.

Figure 8 is an example of a portion of an entity-relationship data structure that can integrate multiple biological/chemical databases according to some embodiments of the invention. In Figure 8, the entities or nodes, represented by the ovals, contain a

quoted string specifying their category (e.g., "gene"). The lines between the nodes indicate parental relationships (also referred to as group membership), with the parent groups displayed higher in Figure 8. The text items connected to the entities are their aliases, which show the naming system (e.g. EMBL, SWISS-AC) and the identifier within that naming system. There are two proteins in Figure 8, and both are referenced by the same Medline article. However, only the protein on the right of Figure 8 has an associated Pfam domain. Below the proteins in Figure 8 are the genes that translate to the protein.

As was described above, some embodiments of the present invention can identify and merge records in a plurality of biological/chemical databases that represent the same entity. Since identifiers within a naming system are considered to be unique, two objects with the same naming system-identifier pair are considered to be identical. In some embodiments, as was described in connection with Blocks **608** and **610**, a record will be added and have an identity cross-reference, also referred to as an alias, to a record that has already been incorporated. When an alias is attached to an entity, some embodiments of the invention can check if the exact naming system-identifier pair is already in use. If it is, the entities are merged together, creating a new entity with all of the relationships, aliases and properties of its component entities.

It also will be understood that databases that are integrated according to some embodiments of the invention can be updated often, in some cases weekly or even daily. If new records are added to the databases, embodiments of the invention can add more entities, aliases and/or relationships. Other embodiments may remove or delete references or entries from databases as was described in Blocks **612-618**. Deletion may not be explicit - that is to say, there may be nothing in the data file that states, "Entry ABC was removed". Instead, the entry may not be present in a subsequent version of the database. Some database vendors, (e.g., GCG's SeqStore product) may approach this issue by rebuilding the entire database with the new data on a regular basis. Unfortunately, this can break relationship links to private annotations that the user might have added, and may even remove these annotations altogether. The total rebuild also may be time-consuming.

According to some embodiments of the invention, deletion may be handled by tagging every alias and every relationship with the database from which it came (the source) and the date of its last update. When a record is read in, some embodiments

of the invention can find the entity to which it points and can check the aliases and relationships to see if any of them have the same source as this record. If any aliases or relationships are found which have the same source, but are not in this record, it is determined that they were removed from the record (Block **612**) and they can be removed from the database (Blocks **614** and **616**) without the need to impact the data that came from other sources.

Moreover, according to other embodiments of the invention, when deleting a record/alias, a situation may occur where two entities had been merged because of a cross-reference, but this cross-reference is later deleted. In this case, some embodiments of the invention may need to determine whether or not to split the entity into several other entities, and which aliases each should have (Block **618**). This determination can be thought of as a graph theory problem, which can be solved by determining the transitive closure of the aliases (as nodes) and the update information (as connections). The existence of a connection between two aliases can be used as an indication that they belong in the same entity. If all the aliases belong in the same entity then a split may not need to be made.

The following Examples shall be regarded as merely illustrative and shall not be construed as limiting the invention. These Examples represent data management problems for which some embodiments of the invention may be used. In the Examples, a description is provided of how one may approach the problem using embodiments of the invention, a link-federated database and a data warehouse. In these Examples, the user may be a bench scientist with a vague understanding of bioinformatics, but with no programming or database administration skills.

Example 1 - Translation

The user is experimenting with bonobo apes. There is a bonobo ape database (BonoboBase), which is not in the user's database, but the user has a table of links (BonoboToGenpept.txt) between BonoboBase and a peptide database GenPept. The user wishes to compare a Bonobo microarray experiment, which has BonoboBase numbers, and a human microarray experiment, which has Genbank Accession numbers.

Using some embodiments of the invention: Since GenPept and Genbank may be cross-referenced by some embodiments of the invention, all that may need to be done is add another alias to these records. The user can run a translation table filter

program, and can specify BonoboToGenpept.txt as the input file. Now that the aliases have been added, the user can run a translate file feature as many times as the user wishes to translate the Bonobo microarray experiments to Genbank numbers.

Using a link-federated database: Although the user may get the data file into the database and look at it, automatic translation may not be possible using a link-federated database.

Using a data warehouse: It may be difficult to easily add the new data to the database. The user may have to get a database administrator to create a new set of tables for BonoboBase records, which may be joined to the table of GenPept records. Because there is no grouping, a custom script may then have to be written for this specific type (BonoboBase to Genbank, through GenPept) of translation.

Example 2 - New Experiment

The user decides to screen compounds against some bonobo genes. The user devises a system wherein the user can label each gene-compound interaction with either 'effect' or 'no effect'. When the user acquired the database, the user didn't anticipate performing compound screening, and didn't ask for this feature. Now the user wants to search the database for all the genes in the kinase family that are affected by ethanol.

Using some embodiments of the invention: If the user's file is in tab-delimited (for example, an Excel text file) format, in XML format, or in any other format it can import, programming or data structure modification may not need to be done. The user can then search for genes in the kinase family affected by ethanol.

Using a link-federated database: The data can be added by creating a new template for the new format. However, complex queries such as this one may not be possible in a link-federated database because connections generally are hyperlinks and may not be usable in searches.

Using a data warehouse: Again, it may be difficult getting the data into the database. Since the user did not request support for this particular type of data in the beginning, the database structure may need to be modified to add the data. Once this has been done, searches such as the one described can be performed.

Example 3 - Unsupervised Explanation

The user takes a treatment series experiment and uses hierarchical clustering to arrange the data. The user looks at the genes and identifies a sub-tree containing genes that are all decreasing in expression over time in a highly correlated manner. Now that the user has a list of genes, the user wants to know why they would be clustered together in this experiment.

Using some embodiments of the invention: The data in the entity-relationship model can be typeless, so one can search for shared groupings of any type with a single query. Using a query tool, the user can enter the gene names, and may be given a result such as "80% of these genes are in the Prosite family EF-hand".

Using a link-federated database: Such queries may not be possible in this type of database. The user may enter the names of the genes one by one, look at the records, write down the families/references/etc. and look over it manually to determine if they had anything in common.

Using a data warehouse: Since a data warehouse is based around specific tables for specific data types, a typeless grouping search may not be able to be performed. The closest approximation may be a supervised approach, where the user may phrase the question as "What Prosite grouping do these genes share?" Since there are hundreds of possible types of groupings, asking this question for every single one may be extremely tedious.

Example 4 - Distant Relationship

The user conducts an experiment, which leads the user to believe that Protein CSR2_RAT is connected to Leukemia. The user cannot, however, find any literature or references to confirm this, and wants to search the database for any possible indirect links between CSR2_RAT and Leukemia.

Using some embodiments of the invention: The user can use a relationship finder tool and enter the *CSR2_RAT* and *Leukemia*. Some embodiments of the invention can perform a breadth-first search, traversing any kind of relationship and can tell the user that "CSR2_RAT shares Pfam: LIM with RHM1_HUMAN. RHM1_HUMAN is related to OMIM-DISEASE: Leukemia".

Using a link-federated database: Once again, the task of searching the database for a connection may become a tedious process of clicking between pages,

hoping to find some relationship. It may be difficult to do this automatically, except perhaps using a Web crawler.

Using a data warehouse: As with the previous Example it may be very difficult to perform an unsupervised traversal of the data because it generally is contained in tables of specific types with specific relationships. While the user can ask "Does CSR2_RAT share a Pfam domain with a protein related to Leukemia?", the user may not be able to simply say, "Find the relationship." This may make the search extremely tedious, and it may be virtually impossible if there are more than two steps involved.

Example 5 - Multivariable Cluster Analysis

The user would like to look at the hierarchically clustered expression data and understand how the clusters relate to molecular function in the Gene Ontology.

Using some embodiments of the invention: The user can enter clustered expression data and select Molecular Function as a second view. The user then may get a display showing the expression-clustered data in one panel and the same genes as are in this experiment clustered by molecular function in another panel. When the user moves the mouse over a subtree in one panel the genes in the subtree may be highlighted in both panels so that the user can explore and make hypothesis about the relationships between function and expression in the experiments.

Using a link-federated database: It may be possible that a program could be written to retrieve every gene record specified in the user's file and the group them by common references. However this may require that there were no levels of indirection (i.e., the gene records directly reference by what they are to be clustered), which is not the case in the Gene Ontology, and that the structure of the tree was flat (i.e., not a hierarchy or ontology).

Using a data warehouse: This may be possible, if the data warehouse was designed to support all the levels of the ontology data.

The above Examples illustrate that embodiments of the invention can provide translation among naming systems, allowing cross-referencing and clustering of experimental and/or public data. Data types that have never been seen before can be added. Aliasing and grouping can reduce multiple levels of indirection to a single reference. Complex queries may be performed and typeless data may be used.

It also will be understood that although embodiments of the invention have been described above with respect to genes, proteins, literature references, domains, ontologies and other data types, the ways in which data can be categorized and cross-referenced using embodiments of the invention can be virtually unlimited. For example, the description lines of genes from Hugo may be used in order to group them into sets of mutant alleles. A combination of Medline and expression data may be used to infer groupings on the basis of likely interactions. Also, high-throughput screening data may be used to cross-reference chemicals to genes and then group the chemicals by structure. Many other databases also can be used.

The application space for embodiments of the invention also appears to be varied and widely unexplored. Embodiments of the invention can allow a user to perform searches and analyses that previously may have been unavailable or at least very difficult to implement. There are many more applications beyond those described here. Embodiments of the invention can include both remote and local APIs with many powerful functions, both for internal use and to encourage development of applications.

Figure 9 is a flowchart of operations for integrating biological/chemical databases according to other embodiments of the present invention. As will be described below, these embodiments can create an ontology network from a plurality of independent ontologies, to thereby provide a foundation for discovery.

In particular, referring to Figure 9 at Block **902**, an entity-relationship model is obtained for each of the plurality of biological/chemical databases. It will be understood that the entity-relationship model may be available as part of the database schema of each of the biological/chemical databases so that it merely may need be received. If not, an entity-relationship model may be created using known techniques. Accordingly, the word obtain, as used herein, includes receiving an existing entity-relationship model and/or creating an entity-relationship model.

Then at Block **904**, at least some of the related entities in the entity-relationship models in at least two of the biological/chemical databases are identified. At Block **906**, the related identities in the entity-relationship models in the at least two of the biological/chemical databases are linked, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases and creates an ontology network. Operations at Blocks **904** and **906** are repeated until a plurality of related entities, and in some embodiments all related entities, are

identified and linked. Once the ontology network is created, a query may be performed by performing operations of Blocks **512-520**, as were already described. This description will not be repeated for the sake of brevity.

In some embodiments of the invention, the related identifies are identical entities that are linked by merging into a single identity. In other embodiments, the related identities need not be identical. In particular, in some embodiments, entities which are similar but not identical may be associated with one another through a relationship type. The two entities may share aliases, inherit relationships from one another, and may share all benefits of a merge, but may remain separate entities. In other embodiments, entities which are similar but not identical may be associated with one another through a parent entity. All of the identical information may be contained in the parent entity in these embodiments, while the differential information is contained in the child entities. Common relationships are inherited through the parent entity, while relationships particular to the child entities are not. Finally, in still other embodiments, entities which are deemed to be related through traversal may be associated through the construction of a meta-relationship which encapsulates the multiple relationships along the original traversal. Yet other examples of linking of related entities may be provided, according to other embodiments of the invention.

Referring now to Figure 10, operations for integrating a new biological/chemical database into a plurality of biological/chemical databases according to some embodiments of the invention now will be described. In particular, as shown at Block **1002**, an entity-relationship model is provided for the plurality of biological/chemical databases. The entity-relationship model links at least some related entities in at least two of the biological/chemical databases. This entity-relationship model may be obtained, for example, by performing the operations of Blocks **902-906** of Figure 9.

Still referring to Figure 10, at Block **1004**, an entity-relationship model for the new biological/chemical database is obtained. At Block **1006**, at least some of the related entities in the entity-relationship model for the new biological/chemical database and the entity-relationship model for plurality of biological/chemical databases are identified. If related entities are identified at Block **1006**, the identical entities in the entity-relationship model for the new biological/chemical database and the entity-relationship model for the plurality of biological/chemical databases are linked.

For example, in some embodiments, at Block **1008**, the identical entities in the entity-relationship model for the new biological/chemical database and the entity-relationship model for the plurality of biological/chemical databases are merged into a single entity. Also, in some embodiments, at Block **1010**, a plurality of aliases are established for the entity that is merged, a respective one of which points to a respective one of the identical identifies in the entity-relationship models in the at least two of the biological/chemical databases. The identification of related entities, merging and establishing of aliases (Blocks **1006, 1008** and **1010**, respectively) are continued, until a plurality, and in some embodiments all, related entities have been identified and linked. Operations for deleting records also may be performed at Block **612-618** as was described above.

Referring now to Figure 11, a plurality of biological/chemical databases may be queried according to some embodiments of the present invention, by providing an ontology network that links at least some related entities in at least two of the biological/chemical databases at Block **1102**. This ontology network may be provided by performing the operations of Figures 9 and/or 10. Querying may be performed by performing the operations of Blocks **512-520**. These operations will not be described again for the sake of brevity.

Additional qualitative discussion of creation of an ontology network according to some embodiments of the present invention now will be provided. Some embodiments of the invention can overlay/merge/associate ontologies and provide extensive cross referencing to other existing data bases, data tables, data repositories, and ontologies. According to some embodiments of the invention, the resulting knowledge layer can provide an ontology network where multiple ontologies and various entities have been linked. The ontology network can bridge previously disparate data repositories, bringing structure to a previously amorphous assembly of independent ontologies of entities and relationships.

According to some embodiments of the invention, this ontology network can provide multidirectional characteristics of parent-child relationships. Specifically, the relationships that hold among the objects or entities of an ontology network can be said to have a character where each entity may have another entity from which it was derived or have or is assigned hierarchical characteristics with regard to another entity. However, since an ontology network need not be limited to this form, other new relationships or hierarchies can be created by the process of overlay, merge

and/or association of entities from other ontologies of interest. This conceptualization of knowledge may be constructed of knowledge from objects of similar domain and can serve as a specification mechanism for the development of a mesh belief system that can deliver experimental insight. This system may provide for the ability to traverse and thereby establish a linked path of relationships creating associations between characteristically unlike entities and also may provide for the revelation of new information and knowledge. The resulting lattice of semantically rich metadata can form an ontology network that can capture the knowledge from the data sources it supports.

According to some embodiments of the invention, an ontology network **210** can reside as a part of an information stack related to the basic scientific experiments where enormous quantities of data are collected, for example as was shown in Figure 2. In some embodiments, the ontology network can be located above a conventional integration tool or layer **206** and can provide a knowledge mining tool or layer **110** that can be available for hypothesis or question-driven mining as opposed to complex data mining queries typical of data mining applications. Some embodiments of the ontology network can comprise a meta database of terms, entities and/or data relationships that can provide for a more efficient and intelligent analysis of accumulated data.

According to other embodiments of the invention, implementation of virtual experiments **112** and discovery **212** that employ this ontology network can provide inference engines. As is well known, the components of an expert system are a knowledge base, which may be implemented according to embodiments of the invention by an ontology network **210**, and an inference engine which performs reasoning. According to some embodiments, an inference engine or reasoning software application searches and creates rules by determined pattern matching and then establishes new rules and develops forward chaining of rules. Virtual experiments **112** within the subject field of inquiry can be executed which can significantly enhance accuracies and/or have abilities to correlate observations to original predictive behavior with a broader input of related information than previously may be employed.

Inference engines can be made more accurate as a result of the type designation of relationship, building of newly determined relationships, along with the quantification of the confidence and/or validity assigned to these relationships. As

will be described below, some embodiments of the invention can assign confidence to different traversals and/or variations in selected paths as they are determined or discovered. This characteristic of an ontology network according to some embodiments of the invention can be further integrated into use by the creator of the virtual experiment to add greater value and relevance to data across the broad span of information among the many domains made available in this semantically rich metadata layer.

As was described above, according to some embodiments of the present invention, an ontology network is created by merging, overlaying and/or linking identical objects and/or establishing a relationship between objects/entities in different ontologies. Figures 12-17 conceptually illustrate an example of the creation of an ontology network according to some embodiments of the present invention.

In particular, Figure 12 depicts an ontology that is linked to data fields known to relate to molecular function. Thus, Figure 12 depicts a molecular function ontology **1210**. One specific example of such an ontology is the GO Consortium function ontology. In this ontology, relevant data exists where the gene sequence ID **1220** or the protein ID **1230** encoded by the gene sequence has a known function in some physical location **1240** and/or in a particular tissue **1250**. The gene sequence ID **1220** also may be linked to raw sequence data **1260** in the molecular function ontology **1210**.

Figure 13 illustrates a biological process ontology **1310** which also links to a gene sequence ID **1320**, a physical location **1340**, a tissue **1350**, raw sequence data **1360** and a protein ID **1330**. Figure 14 illustrates a cellular component ontology **1410**, which also links to a gene sequence ID **1420**, a physical location **1440**, a tissue **1450**, a protein ID **1430** and raw sequence data **1460**.

Figure 15 illustrates the linking of the multiple ontologies of Figures 12, 13 and 14 into an ontology network by identifying an identical entity gene sequence ID **1520** and using the identical gene sequence IDs **1220** of the molecular function ontology, **1320** of the biological process ontology and **1420** of the cellular component ontology, to link the molecular function ontology **1210**, the cellular component ontology **1410** and the biological process ontology **1310** into an ontology network by reference to the gene sequence ID. A specific example of the linking of Figure 15 may include the three separate GO consortium ontologies and a linkage via SWISS-PROT database entries according to some embodiments of the present invention.

Operations of Figure 9 may be used in some embodiments to link these disparate ontologies.

Figure 16 illustrates an example of another ontology **1610** for protein function, including a protein ID **1630**, a gene sequence ID **1620**, a physical location **1640**, a tissue **1650** and raw sequence data **1660**. Figure 17 illustrates adding the ontology **1610** of Figure 16 using the gene sequence ID entity **1720**, for example using operations of Figure 10.

As was described above, an ontology can be thought of as a knowledge construct that contains therewithin an answer to a question or a set of beliefs particular to a given domain. Thus, in the example of Figures 12-17, ontologies about biological processes may aid in the determination of what protein might play a role in a particular process. The combination of ontologies results in the creation of an ontology network in Figures 15 and 17, which can yield answers to questions that were not originally expressed by any of the original ontologies as conceived. Thus, an ontology used to express a belief about system **A**, and an ontology used to express a belief about system **B** can be associated together according to embodiments of the present invention, to express belief about systems **A** and **B**, but to also answer a new query **C**.

For example, Figure 18 illustrates a query **1810** that can be run by traversing the ontology network of Figure 17. The query can reflect a belief that, for example, nucleic membrane genes are more likely to create protein kinases than anything else. By traversing the ontology network of Figure 17, the cellular component ontology **1410** can reveal which are the nucleic membrane genes, and the molecular function ontology **1210** can reveal which are protein kinases. Since these two ontologies are now linked in an ontology network, an answer to the query may be provided. Thus, an ontology network according to some embodiments of the invention can allow a user to form hypotheses about the role of function in process, or of process in function. Many other hypotheses may be formed.

It will be understood by those having skill in the art that Figures 12-18 illustrate a relatively simple example of linking of ontologies to provide an ontology network. An example of the complexity of linkages that may be available according to some embodiments of the invention is illustrated in Figure 20. The intensity of the implied web created by this network of linkages can continue to develop. The development of density may result in yielding and revealing accurate and relevant

knowledge to accelerate the organization of knowledge. Increased density of relationships between entities, data structures, and ontologies may result in the acceleration of knowledge and the discovery process.

In particular, Figure 19 illustrates an ontology network comparing the Stanford GO Cell Component Ontology and the Stanford GO Biological Process Ontology. In Figure 19, the Stanford GO Cell Component ontology references the same proteins as the Stanford GO Biological Process Ontology, allowing the traversal from structure to function that is shown in Figure 19.

Figure 20 is presented as an example of the linkages displayed in Figure 19 and the organization and resulting increased perspective that may be provided by some embodiments of the invention to reveal relevant information surrounding one entity. Some embodiments of the invention can reorder these cross-references in a manner that may enable the mining of vast amounts of information, literally files of data, quickly and easily, without the need for a deep understanding of any of the databases that are included, or of the complex data-mining techniques applied in the back-end. Users may interact with a logically crafted front-end (interface) that provides access to the complete ontology network, without overwhelming users with complex technical queries.

Figure 21 illustrates another example that uses aliases to provide a network of ontologies according to some embodiments of the present invention. In the case of the heredity breast cancer gene, the multiple aliases of related protein and sequence that encodes it, is shown, and a resulting browser view of the gene, protein and sequence is also shown. The browser is an exemplary query tool of the ontology, and can display the many links and alias examples created in the construction of Figure 20 in a potentially easy to understand and intuitive view. Thus, in some embodiments of the invention, the power of the ontology can hide the vast knowledge that is stored in its relationships and constructs.

Figure 22 is a block diagram of a data processing architecture that may be used with some embodiments of the present invention. In particular, the construction of expert systems has been the subject of research in computer science. The creation of a knowledge layer, where a significant responsibility beyond simple reasoning is applied to the inference engine, may need to use supercomputing capabilities. In creating ontology networks according to some embodiments of the present invention, it may be desirable to access significant computing resources. The quantity and time

to complete the construction of such an ontology network may be tied to the volume of data in the repositories to be supported by the ontology network and the available computer resources applied during the construction of the metadata referencing the data repositories. Resources ranging from about 30 – 50 gigaflops may be employed in some embodiments, to construct an ontology network in a reasonable time, such as days. Resources ranging up to about 100 gigaflops or more may be used in some embodiments to construct an ontology network to support larger repositories. A computational system able to support more than 100 Gigaflops of computer power may be among the top 500 supercomputers presently available.

In some embodiments, the creation and/or execution of the ontology network may use peer-to-peer or grid computing technology. Here, processing cycles from many computers on a network are harnessed, and the application used to create the ontology network may be "gridified" to make the best use of these resources. The construction of such a knowledge layer may be well suited to distribution of the millions of small processes. As a result of increasing efficiencies and decreasing costs to employ computer resources as a grid, the construction of such a meta database that captures the information content of the underlying repositories may become a common part of the mining of complex and disparate data systems. The design and operation of peer-to-peer computing systems are well known to those of skill in the art and need not be described further herein.

An example of a database schema which can be used in an ontology network engine, such as an ontology network engine **300** of Figure 3 or **400** of Figure 4, to store metadata concerning diverse databases in a metadata database such as the metadata database **308** of Figure 3 or **408** of Figure 4, now will be described. It has been found, according to some embodiments of the invention, that the metadata can be stored in a generic database using a conceptual schema that can be implemented using conventional relational database management systems, such as Oracle, MySQL and/or Access.

It will be understood by those having skill in the art that database design may refer to a conceptual schema that exists between the external perception of data (often referred to as an external schema) and the internal on-disk view of data (often referred to as an internal schema). This three-schema architecture conceptualization can enable a programmer to abstract and create various external views of data from the internal view. The conceptual schema can be a composite of all external schemas,

such as the use of tables and columns in a spreadsheet, so that external views can be derived from the conceptual schema, while providing the translation for data recording to the physical schema or on-disk structure.

Referring now to Figure 23, according to some embodiments of the invention, a conceptual schema for an ontology network can itself be embodied as an entity-relationship model. In Figure 23, the individual boxes may represent tables in a MySQL database. These tables are logical groupings of related data. The lines between the boxes represent relationships between common information or cross-references between distinct tables. The entries inside each box represent unique keys or columns of data for each piece of data held by that table or piece of data.

In particular, referring to Figure 23, the boxes enclosed by dashed Block **2310** may be used to define entities including the entity name, entity category, attributes or properties of the entity, and aliases of the entities. The boxes enclosed in dashed Blocks **2320a** and **2320b** may be used to define relationships, including an identification of the relationship, the attributes or properties of the relationship, and the type of the relationship. The boxes enclosed by dashed Block **2330** define user interface aspects including security aspects. The boxes enclosed by dashed Block **2340** define Uniform Resource Locators (URLs) for external databases that may used with an entity browser. The boxes enclosed by dashed Block **2350** provide functionality for updating the ontology when a new version of a database is input. Finally, the box enclosed by dashed Block **2360** defines the applications that can be used with an ontology network. It will be understood that at database schema of Figure 23 may be used by those having skill in the art to create a relational database using a conventional database management tool.

Thus, the database schema of Figure 23 is itself represented by an entity-relationship data model. The entities may hold information and may stand alone, or may have relationships between other entities holding data. Thus, the conceptual schema of Figure 23 illustrates the existing relationships that are declared as being true for the data before discovery of new relationships via inference and/or results are presented. This conceptual schema may be used to create a relational database that can provide a network of ontologies according to some embodiments of the present invention.

Referring now to Figure 24, operations for integrating biological/chemical databases and integrating new biological/chemical databases according to other

embodiments of the present invention now will be described. These embodiments assume that database records are provided via XML text records. The use of XML text records and the conversion of non-XML records to XML records are well known to those having skill in the art and need not be described further herein. Moreover, it is assumed that the loader, such as the loader **302** of Figure 3, that is used to load the XML text records also has knowledge of the ontology's semantics based upon the ontology's external data files. As was described above with respect to Figure 23, the ontology semantics also may be extracted from an external biological/chemical database, if they are not already known. Accordingly, *a priori* knowledge of the ontology's entities and relationships is known at the time of loading.

Referring now to Figure 24, operations begin with an XML description of an entity in a biological/chemical database at Block **2402**. At Block **2404**, the XML description is read. At Block **2406**, a list of aliases is obtained from the XML description. At Block **2408**, a test is made as to whether an entity with one of these aliases already exists in the network of ontologies. If yes, the existing entity is obtained at Block **2412**. If no, at Block **2414**, a new entity is created. Source information then is obtained from the XML text at Block **2416**.

Continuing with the description of Figure 24, operations for adding the aliases from the XML input to the entity and merging the entity with other entities when the aliases match now will be described. In particular, for each alias in the XML text file (Block **2418**), the alias and the source information are added to the entity at Block **2422**. At Block **2424**, a test is made as to whether the alias exists in another entity. If yes, the other entity is merged with this one at Block **2426**. A test is then made at Block **2428** as to whether any aliases remain and, if so, the operations of Blocks **2418-2426** are repeated until none remain.

Operations continue at Figure 25. At Block **2502**, parent relationships and associated source information are added to the entity and at Block **2504**, parent relationships that no longer exist are removed from the entity. At Block **2506**, child relationships and associated source information are added to the entity and at Block **2508**, child relationships that no longer exist are removed from the entity. At Block **2512**, the attributes are added or updated to the entity.

Still continuing with the description of Figure 25, operations to remove aliases from the existing entity that no longer appear in the XML input now will be described. In particular, for each alias in the entity (Block **2518**), a test is made as to

whether this alias exists in the XML text file at Block **2522**. If not, the alias is deleted from the entity at Block **2524**. Moreover, as a result of deleting the alias from the entity, a test is made at Block **2526** as to whether the entity needs to be split due to the alias deletion and, if so, the entity is split at Block **2528**. The operations of Blocks **2518-2528** are completed until there are no aliases left at Block **2532**, whereupon operations end.

Accordingly, Figures 24 and 25 illustrate operations for inputting data into the ontology network via an XML text record according to some embodiments of the present invention. During these operations, new entities are constructed and merged, to achieve linking and merging of previously disparate entities. The addition of an ontology may be executed in the same manner. In particular, elements of the ontology are read and operations of Figures 24 and 25 are followed.

For the purpose of loading an ontology into a preexisting network of ontologies, care may need to be taken because entities within the new ontology may have relationships pointing to other entities within the ontology network, and may also have relationships to entities already existing in the ontology network. The operations that were described above in connection with Figure 25 can maintain consistency. Thus, Figure 25 provides embodiments of operations for building new or adding parent and/or child relationships. Removing aliases that may become out of date as a result of an update process also was described. Other new types of relationships, such as reaction right or reaction left or reaction forward or reaction back also may be added, to provide an ability to filter by step.

The following Table describes algorithms that may be used according to some embodiments of the invention, to add an entity and add a relationship using the database schema of Figure 23 and the operations of Figures 24 and 25:

Table

Adding an Entity

Overview

Add the entity information.

Add an updateInfo for the entity from the external data source.

Why updateInfos: to differentiate data from different external data sources in order to handle data inconsistency between those sources.

Once in the system, information cannot be deleted until all external data sources that put it there agree that it no longer exists.

UpdateInfos are associated with aliases and relationships.

Add Aliases to the entity.

The updateInfo is used when adding aliases.

Add the Entity Information.

Algorithm

Add this entity's category to the category table if it is not already there.

Add this entity's information to the entity table.

Add this entity's attribute information to the entity property table.

Modified Tables

IcCategoryList

New row added with the entity's category if the category doesn't already exist.

IcEntity

New row added with the entity's information.

IcEntityProperty

New row(s) added with the entity's attribute information.

Add an UpdateInfo for the Entity from the External Data Source.

Algorithm

If the updateInfo is already in the updateInfo table, update its date information.

Otherwise, add the updateInfo information to the updateInfo table.

Modified Tables

IcUpdateInfo

New row added with the updateInfo's information.

mLastUpdated column updated with the date information if the updateInfo is already in the table.

Add Aliases to the Entity

Algorithm

If the alias is already in the database attached to another entity, then merge that entity with this alias's entity.

This involves taking all the data for the two entities pointed to by the alias and putting it on a single entity, then removing the other entity from the system.

Otherwise add the alias's information to the Alias table.

Associate the specified updateInfo with the alias.

Modified Tables

IcAlias

New row added with the alias's information.

IcAliasUpdateInfo

New row added to associate the updateInfo with this alias.

IcTypeList

New row added with the alias's type if the type doesn't already exist.

Modified Tables Due To Merging Entities

IcAlias

IcEntityID column changed to point the alias to the merged entity.

IcEntity

Existing row for the old entity deleted.

IcEntityProperty

Existing row(s) for the old entity attributes deleted.

IcEntityID column updated to point to the merged entity.

IcRelationship

Existing row(s) for relationships on the old entity deleted.

ParentIcEntityID column updated to point to the merged entity.

ChildIcEntityID column updated to point to the merged entity.

IcRelationshipProperty

Existing row(s) for attributes on relationships on the old entity deleted.

IcRelationshipUpdateInfo

Existing row(s) for updateInfos on relationships on the old entity deleted.

IcRelationshipID column updated to point to the merged entity.

IcUpdateInfo

IcEntityID column updated to point to the merged entity.

Adding a Relationship

Overview

Add the Relationship.

A relationship is added between two already-existing entities.

One entity is the parent, the other is the child.

Each relationship has an associated UpdateInfo for the external data source.

Add the Relationship.

Algorithm

If a relationship of this type already exists between the parent and child, update that relationship's information.

Otherwise add the relationship's information to the relationship table and its attributes to the relationship attribute table.

Associate the specified updateInfo with the relationship.

Modified Tables

IcRelationship

New row added with the relationship's information.

IcRelationshipProperty

New row(s) added with the relationship's attribute information.

IcRelTypeList

New row added with the alias's type if the type does not already exist.

IcRelationshipUpdateInfo

New row added to associate the updateInfo with this relationship.

Querying of ontology networks according to other embodiments of the present invention now will be described. In particular, Figures 5, 7, 9 and 11 described embodiments for querying the ontology network according to some embodiments of the present invention. However, it will be understood that ontology networks according to some embodiments of the present invention can provide a large number of associations among a large number of entities in diverse ontologies. In some embodiments, discovery may take place by querying the ontology network to traverse the ontology network from one entity to another. Stated differently, in some embodiments, a starting entity and an ending entity may be specified, and the query results can provide some or all of the paths that can link the starting entity to the ending entity, to thereby obtain new discovery.

Unfortunately, due to the large number of linkages between entities that may be provided when building real-world ontology networks, the number of paths which link a starting entity to an ending entity may be inordinately large. In these situations, it may be difficult to obtain discovery by merely traversing the entities, as was described, for example, in Block **516**, due to the large volume of related entities and relationships that may be obtained. However, as will now be described, some embodiments of the invention can provide predefined path rules (Block **324** of Figure

3) and/or user-defined path rules (Block **322** of Figure 3), and allow traversing the ontology network using these path rules as was described at Blocks **514-520**.

More specifically, path rules can specify a type of path to traverse, in response to a given type of query. For example, a path rule may specify a specific type of traversal and a specific type of end point for a specific type of starting point. The path rules can be relatively simple, as was described above, but also can be more complex, involving iterations and/or branching. These path rules can, in effect, create new ontologies within the ontology network based on the belief system of the creator(s) of the predefined or user-defined path rules. *A posteriori* knowledge of the relationship between the disparate ontologies may be built into the path rules that are developed to traverse the ontology network. Path rules may be devised with specific semantics in mind based on the data loaded into the ontology network. Thus, the relationships generated when a path rule is applied to a specific starting entity can have a well defined meaning.

Figure 26 illustrates operations that may be performed to traverse the entities in an ontology network using path rules, according to some embodiments of the present invention, as was generally described at Block **518**. In particular, referring to Figure 26, at Block **2610**, a path rule is obtained either by a user defining a path rule (Block **322**), or by obtaining a predefined path rule (Block **324**). At Block **2620**, the path rule is applied to a specified start point. At Block **2630**, the end point or end points found by the path rule are obtained. At Block **2640** a test is made as to whether additional start points are present. If not, at Block **2650**, the results of the query may be provided.

Moreover, as also shown in Block **2650**, in other embodiments, the start points and end points that are now linked by the path rule can be used to define a new ontology, and can be stored in the metadata database to become a permanent part of the ontology network based upon the belief of the user of the ontology network, rather than merely being a temporary result of a query. In particular, at each step of the traversal through the entities that comprise an ontology network, decisions are made regarding which relationship is selected. Thus, the establishment of a belief at each step or traversal of the system begins to establish multiple steps of order. A decision regarding which step is next in a traversal may be implemented, according to embodiments of the present invention, by providing filtering in the path rules, to thereby create an overall path rule.

Moreover, once a new relationship is declared that is comprised of other steps in the traversal, these rules can be applied by the external schema. Alternatively, they can be physically applied to the internal schema. In other embodiments, a path rule need not persist or be part of the internal schema. Rather, knowledge mining only may need to enable the presentation of this order to the user's results of a study.

At the point of validation of a path, results may yield significant knowledge regarding an entire system of knowledge that is now resident in an ontology network. Thus, with the application of filtering in the path, execution of path rules and/or global filtering according to some embodiments of the present invention, an ontology network can become more than an amorphous set of entities and relationships, and can become more of a rich knowledge base with inherent discoveries therein.

Accordingly, some embodiments of the invention store the query results that are based on the entity-relationship model of the plurality of biological/chemical databases as at least one new relationship in the entity-relationship model, to thereby store knowledge that was derived from the query in the entity-relationship model of the plurality of biological/chemical databases. The ontology network, therefore, can expand based on the knowledge that was obtained as a result of querying the ontology network. In other embodiments, these query results are not stored, so that the query results are not used to modify the ontology network itself.

Filtering according to some embodiments of the invention may specify a relationship type, such as part of, derived from, forward reaction or reverse reaction. Filtering according to other embodiments of the invention also can include or exclude specific types of entities, such as symbols or reactions. Filtering according to yet other embodiments of the invention may also filter on a relationship attribute, entity attribute, alias type, alias ID, category, relationship-type confidence, parent-child, self, and/or other characteristics. Thus, filtering on each step of the traversal can create a preselected path that is acceptable or unacceptable relative to the confidence of the relationship, or as simple as the direction of reaction catalyzed by an agent.

Figure 27 provides an example of an *in silico* experiment that can be derived from an ontology network according to some embodiments of the invention. The example in Figure 27 begins with an experiment **2702**, such as two GenBank IDs that both express in an expression data experiment. The remaining blocks of Figure 27 illustrate a path route taken from the starting GenBank ID to the ending GenBank ID. Running the experiment in an ontology network according to some embodiments of

the present invention can validate the path. Moreover, repetition of the path illustrated in Figure 27 across the entire contents of the ontology can implement long-range order in the ontology network and create knowledge and/or values of many other GenBank IDs. A path, such as a path described in Figure 27, can be incorporated into the ontology network, so as to allow this path and all related paths to persist. This can add another ontology to the ontology network according to some embodiments of the invention. Alternatively, in other embodiments this path can be recognized as part of the external schema, and reported as a query result. In either case, a single verified and validated segment of knowledge can be multiplied by inference, and can yield answers to questions or experiments not yet run.

Figures 28-35 provide another example of a path rule that may be used to obtain discovery according to some embodiments of the present invention. In particular, Figure 28 illustrates a small portion of an entity-relationship model that is part of an ontology network according to some embodiments of the present invention. As shown in Figure 29, this example of a path rule can start with a general protein function **2910**, and can find the proteins with that function (Block **3010** of Figure 30). The path rule then can expand the query by finding the processes in which the protein is involved, as shown at Block **3110** of Figure 31. All the proteins in these processes may be examined, as shown at Blocks **3210** and **3220** of Figure 32. Screening data can be traversed for the proteins, as shown at Blocks **3310** and **3320** of Figure 33. A list of chemicals that screen favorably can be retrieved, as shown at Blocks **3410**, **3420**, **3430** and **3440** of Figure 34. Finally, as shown at Blocks **3510** and **3520** of Figure 35, those chemicals with undesirable properties, such as toxicity and/or unwanted structure, can be filtered out.

Figure 36 illustrates an example of a user display screen that may be used to initiate a query using the path rule that was specified in Figures 28-35. Figure 37 illustrates a user display screen of query results that may be obtained.

Figures 38 and 39 are flowcharts of operations for querying an ontology network according to other embodiments of the present invention. Figure 38 illustrates querying from a user perspective. Figure 39 illustrates operations from a client-server standpoint.

According to other embodiments of the present invention, an ontology network can be constructed where the relationships between objects are further labeled and characterized with confidence levels as well as type. The ontology

network may be traversed in response to a query, to thereby obtain query results that are based on the entity-relationship model including the at least one confidence level that is assigned. Inferences and correlations commonly employed in the biotechnology area may be characterized to better enable application of these relationships as a more exact and analytical science. This knowledge may not only be harnessed by reasoning engines to create more valid and accurate virtual experiments, but also new relationships may be discovered, built into the ontology network, and/or learned by the ontology network to establish and discover new correlations. The value or quality of these new relationships can be screened and/or further characterized.

In some embodiments of the present invention, information queries of the ontology network can be exact. Results of queries where the retrieved information appears to have been filtered can result from the deployment of knowledge associated with preselected paths. In conventional data queries, data acquired may be filtered to screen unwanted and incorrect results. Not only may this be time consuming, but often the results may still contain significant error and false information. In contrast, queries constructed and run using preselected paths according to some embodiments of the invention may provide only an accurate and concise representation of the information content of the underlying repositories.

In view of the above, some embodiments of the present invention have recognized the principle that relationships between biological entities may be critical to the discovery process. Embodiments of the present invention can logically organize and cross-reference data into groups, so that the data can be fully accessible and useful. Some embodiments of the invention can merge naming conventions or aliases. Other embodiments of the invention can allow researchers to place proprietary research data into the broadest possible relative context with public research data. Moreover, some embodiments of the present invention can anticipate researchers, think, reduce or eliminate repetitive tasks and/or automate the manual processes that may be used in research and discovery.

Some embodiments of the present invention can merge and adjust multiple ontologies to reflect the rapidly changing state of standards and semantics in the life sciences, so that legacy work and investment need not be lost. Thus, some embodiments of the invention can converge information relating to biological and chemical properties, physiology and/or published research. This information may be

cross-referenced. For example, cross-referenced information from more than twenty public life sciences databases, including over forty naming systems, may be provided in some embodiments of the invention, and links may be established between genes, proteins, biochemical pathways, diseases, organisms, literature references and other entities of interest that are referenced in each included data source.

Accordingly, some embodiments of the invention can merge redundant database entries from different sources into single entities with alternate names or identifiers. Relationships between entities can capture knowledge from different data sources. These entities and relationships can make up an emergent ontology-based network, capturing the concepts behind life sciences databases. This network may not be hard-coded, such that new entity types can be added without the need to modify the underlying database, and relationships between any entities may be allowed. In addition, in many embodiments, entities are sparsely populated, so that only aspects of original data that either involve relationships between entities, or are relevant to user queries may need to be integrated.

Some embodiments of the invention can represent data as entities. Some embodiments of the invention can allow entities to represent any concept or type, including concepts not already represented in the existing entity-relationship model. Because of this, a user can add a completely new concept or type without the need to make changes to the underlying database.

An entity can represent a single concept type or individual of that type. According to some embodiments of the invention, if that concept is present in multiple data sources, the multiple sources are merged into a single entity. For example, the predicted *C. elegans* protein YKD3_CAEEL or Q03561 from SWISS-PROT also is represented in PIR as S28280, and in WormPep as B0464.3 or CE00017. In some embodiments of the invention, these database entries can be collapsed into a single entity with the individual identifies as aliases. In practical usage, a user can access all of the relationships for the entity by querying with any of its aliases.

In some embodiments, information about an entity, such as its description, molecule type, or annotation, is stored in attributes. In some embodiments, entities can have unlimited attributes, and each attribute has a type and a value. As with entities, attribute types can represent any concept, and new attribute types can be added without the need to make changes to the underlying database. Attributes may

store information about an entity for the purposes of searching and filtering, and therefore can be metadata storage containers. For example, a nucleotide entity may have both a description attribute and an attribute "molecule type", indicating whether it is DNA, RNA, mRNA, etc., but may not have its nucleotide sequence as an attribute. Instead, the locations of the original database records may be cross-referenced by the nucleotide entity, providing a way to fetch the sequence if need be. Because of this, in some embodiments of the invention, entities may be sparsely populated.

In other embodiments, entities also may be organized into categories or classes, which, like entity types, can be added without the need to change the underlying database. Categories may be used for broad binning of entities, for example protein, pathway, literature or nucleotide-sequence.

Some embodiments of the invention may be constructed from life science databases that have either cross-references to other databases, or lists of alternate names. When a source is imported, entities may be created not only for the source records, but also for the database records they cross-reference. This can be thought of as a virtual database entry. If at a later time that record is loaded, then its information may be added to the entity in some embodiments. In this way, relationships may be built up from multiple sources.

Entity-relationship models according to some embodiments of the invention also can include relationships, which can allow one entity to represent a group of other entities. For example, a set of enzyme entities can be grouped into a pathway entity. The pathway is the parent of the enzymes, and they are the children of the pathway. The enzymes are siblings of each other. Each enzyme is linked to the pathway by a single relationship, and because there is a parent and a child, it is a directional relationship.

In the above example, an enzyme may be grouped into a pathway. In addition, an enzyme may be grouped with other enzymes having the same function, for example in the EC classification ontology. In this way, an entity can be a member of an unlimited number of groups, and each group can represent a different aspect of its members, according to some embodiments of the invention.

Just like entities, relationships can have a type and attributes, in some embodiments of the invention. The type may be used to describe the action of the relationship (i.e., a gene product is transcribed from a gene, or a gene product is

translated to a protein), while attributes can contain information about the relationship, such as annotation or ontological information (for example, is-a or part-of). Entities can be thought of as nouns, while relationships may be thought of as verbs.

Some relationships may be more certain than others. For example, an enzyme that is known to bind to a ligand is a high quality relationship. On the other hand, if a gene product is said to be related to a protein based on sequence homology of 30%, then that relationship may be of low quality. Therefore, in some embodiments, relationships may have a confidence value to reflect the quality of either the data source or the method used to specify that relationship. Confidence values allow a user to filter out relationships that are of too low quality for their purpose. Because of the confidence values, embodiments of the invention can also be thought of as a DWG.

There can be many sources for relationships in life science databases. For example, SWISS-PROT cross-references EMBL and GenBank entries, that code for its proteins. A Unigene entry points to similar proteins and ESTs. Enzyme entries reference all the proteins with the specified function. A KEGG pathway contains a list of enzymes. Medline entries point to MESH headings, as well as to gene, protein and chemical accession numbers. In this way, a complex network of relationships can be built according to embodiments of the invention. For example, a set of relationships can connect an EST to a gene product, which is in turn grouped under a protein, which is classified as an enzyme with a known function, which has known chemical ligands and is grouped in a pathway. The set of entity- and relationship-types that define the steps to go (in this case) from DNA to chemical ligand provide an example of a path.

The path above starts at a sequence and ends at a chemical ligand while traversing the specified steps in between. Defining this path and traversing it may be a time-consuming lookup task, for example, from a long list of up- or down-regulated genes from a microarray experiment. Manually traversing the path may require looking up entries in multiple databases, from GenBank to Unigene to SWISS-PROT to Enzyme to KEGG and Ligand. Because embodiments of the invention may be a DWG, it can become a graph theoretical operation to automate the process of traversing the path in an efficient manner. In this way, complex cross-referencing tasks may be collapsed into a single operation.

Some embodiments of the invention can use a specification of rules that define paths using XML. A simple rule is a single step, a path rule is multi-stepped, and a branch rule has conditional branching. A full path may contain different combinations of rule types, and a branch or path rule type can have subrules of any type. In addition, each rule can filter by attribute, type or category. The overall specification of a path defines input and output types or categories.

Some embodiments of the invention also can capture ontological relationships implicitly and/or explicitly. In particular, an entity can explicitly represent an ontological concept. In this case, its parents are more general concepts and its children are more specific concepts. A relationship's type defines how a child concept relates to its parent. Concept entities can also represent groups of instances of that concept. In the above example, a DNA polymerase entity constructed from SWISS-PROT has an is-a relationship with the concept entity parent EC:2.7.7.7 (DNA-directed DNA polymerase), and also has a part-of relationship with the parent GO:0006260 (DNA replication). The EC entity has the more general parent EC:2.7.7.- (nucleotidyltransferases), which has the more general parent 2.7.-.- (transferring phosphorous-containing groups). At the top of the hierarchy rests EC:2.-.-.-, which is the general classification of transferases. All of the DNA polymerases grouped under the 2.7.7.7 entity are siblings with the same function, while all of the entities group under GO DNA replication are all siblings in the same process.

Some embodiments of the invention also can define an ontology implicitly. In particular, each entity type and category is a concept, while its relationships define the ontological framework. For example, a protein entity is encoded by a group of gene products, each of which is transcribed from a gene. These relationships are built from the cross-references in life science databases. When a new entity type is added, or an entity is put in a relationship with a previously unrelated entity type, new knowledge about how the different entity types relate to each other may be created.

Since an ontology represents a knowledge domain, an entity that has relationships to entities in more than one domain can bridge those domains. In some embodiments, bridge entities are typically experimental or analytical results. One example is the bridging of biology and chemistry, centered around human beta 2 adrenergic receptor (B2AR) and clenbuterol. SWISS-PROT cites two cloning references that show B2AR is expressed in several tissues, including blood and brain, and is classified by GO as being involved in adenylate cyclase activation. The

SWISS-PROT record points to at least 11 nucleotide sequences for the receptor, and it is classified by Prosite, Interpro and Prints as having GPCR domains. At least two articles referring to this protein are linked to asthma MESH headings, and OMIM links B2AR to asthma as well.

In the chemical domain, it is known that clenbuterol is also known as planipart and clenbuterolum (ChemIDPlus), and it is used as a bronchiodilator (ChemIDPlus). Its structure can be retrieved from ChemIDPlus, which can indicate that the chemical has several functional groups. Fingerprinting analysis can bring up structural similarity to several other drugs, including Albuterol.

To bridge the two domains, experimental data may be used. In this case, text mining of the journal *Biochemical Pharmacology* shows a 70nM binding constant Kd between clenbuterol-(-) and B2AR. In some embodiments of the invention, the domains can be bridged in at least two ways: an experimental result entity can be created that links chemical and receptor, or a relationship between protein and ligand may be created. A path may then be traversed from ligand to protein to disease, and from ligand to clinical application, which can show that clenbuterol is a bronchiodilator used to treat asthma.

Side effects also may predicted: adenylate cyclase activation leads to increased protein kinase A activity (CSNDB), which increases the responsiveness of cardiac muscle to calcium currents (CSNDB). Not surprisingly then, clenbuterol increases heart rate and can in some cases cause cardiac arrhythmia (text mining of HSDB).

Additionally, other structurally similar drugs can be analyzed to anticipate their action. Albuterol, as mentioned above, is structurally similar to clenbuterol. Although there may be no screening data for albuterol, it can be predicted that it is also a beta 2 adrenergic agonist, can be used to treat asthma, and is associated with similar side effects.

Thus, embodiments of the invention can provide context to high-throughput life-science experiments by improving information retrieval, and by enhancing automation and data mining ability. In some embodiments of the invention, new data is merged with existing data, and the resulting entities capture the knowledge and relationships of both sources. Both relationships and entities can have a type for filtering, and attributes for capturing relevant data from original sources. Because of merging and grouping, the resulting ontology network can be more highly connected

than the original data sources, which can allow a path to be found between entities in previously unrelated knowledge domains. Moreover, once a path is defined by a user, it can be used in high throughput analyses, such as a microarray results annotation pipeline.

Additional Examples

The following additional examples shall be regarded as merely illustrative and shall not be construed as limiting the invention. Some embodiments of the present invention can be used to integrate databases other than biological/chemical databases, to create an ontology network. The following additional examples illustrate how three diverse ontologies in the form of databases relating to personal data, securities data and government data can be integrated into an ontology network.

More specifically, referring to Figure 40, one or more databases related to personal data **4010**, one or more databases related to securities data **4020** and one or more databases related to government data **4030** can be integrated into an ontology network **210** by obtaining an entity-relationship model for each of the databases **4010-4030**, identifying related entities in the entity-relationship models of at least two of the databases **4010-4030**, and linking at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of databases. The ontology network **210** may be used for discovery, prediction and simulation **212**, as was already described, for example, in connection with Figure 2.

Figure 41 illustrates a more detailed example of the linking of related entities in entity-relationship models for a plurality of databases. More specifically, Figure 41 provides a simplified entity-relationship model for a plurality of databases related to personal data **4110**, a plurality of databases related to securities data **4120**, and a plurality of databases related to government data **4130**, which may provide an embodiment of databases **4110-4130**, respectively, of Figure 40.

As illustrated in Figure 41, the databases related to government data **4130** may include entities for government statistics that may be published on a regular basis, and that constitute databases of economic indicators that can impact options trading of the ten and thirty year government notes which, in turn, can impact the sales of bonds and mutual fund price shares. In particular, entities for Gross Domestic Product (GDP) **4131**, job growth **4132**, consumer confidence **4133**, weekly retail sales **4134**, earnings and growth **4135**, and monthly retail sales **4136**, are related to an economic indicators entity **4137**.

As is well known to those having skill in the art, the data in the GDP entity **4131** is a measure of the nation's total output of goods and services. The data in the job growth entity **4132** provides an indicator of whether the job market is expanding or contracting. The data in the consumer confidence entity **4133** is an index of consumer sentiment based on monthly interviews with 5000 households. Weekly retail sales data in entity **4134** is reported by the Census Bureau. The Census Bureau also reports monthly retail sales data in entity **4136**. Data for the earnings growth rates entity **4135** is also reported by the federal government.

The entities **4131-4136** are all related to an economic indicators entity **4137**. The economic indicators entity **4137** is linked to a federal discount rate or discount rate futures entity **4140** which also includes a rate history entity **4141** and a guidance entity **4142**. The federal discount rate or discount rate futures entity **4140** is in turn linked to a conference board options value of TNX/TYX (options on the ten year and thirty year rate) entity **4143**. It will be understood that the government data **4130** that is shown at the right-hand side of Figure 41 represents a simplified entity relationship model of many government databases related to economics.

It also will be understood that government data **4130** generally is tabulated in a number of databases on a large number of related and seemingly unrelated topics. In addition to the entities shown in Figure 41, other examples include the money in circulation, M1, M2 and M3, and many other such financial numbers. In addition, the government tabulates crop data, weather statistics, weather forecasting, geothermal, geographic, interstellar, gravitational and commodities data. While this data may be relevant to commodity, futures and option trading, such as takes place at the Chicago Mercantile Exchange or the CBOE Exchanges, experts can create relationships or postulate theories of relationships between many of these data types and factors, and their eventual impact on securities markets and/or the value of particular stocks, bonds and mutual funds containing financial instruments of related companies. These expert traversals and/or relationships can be captured in some embodiments of the present invention, for exploitation and application by expert users and/or by less expert users.

Still referring to Figure 41, an entity relationship model related to securities data **4120** also may be provided. The entity-relationship model related to securities **4120** may include an entity for stock indexes **4121**, an entity for industry indexes **4122**, and an entity for industry sectors **4123**. These entities in turn relate to a

companies entity **4124**. The companies entity **4124** may be related to a corporate bond entity **4127**, which in turn can be related to an interest entity **4128** and a current yield entity **4129**. A mutual bond fund entity **4125** may be related to a mutual fund shares entity **4126**, which in turn can be related to the interest entity **4128** and the current yield entity **4129**.

In particular, many databases exist related to stocks **4121**, bonds **4127** and mutual funds **4126**. Each of these databases may represent an entity type and may be composed of many different company stocks, bonds or fund shares. An example of an extensive database of this type is the Value Line database of stocks. In this example, Value Line has tabulated about 280 financial characteristics or data items of each company in the list. Their list includes about 6000 different companies in different sectors of the economy. These characteristics can include their proprietary characteristics, such as technical rank and safety rank, and general data such as Beta, relative price-to-earnings ratio, earnings-per-share (current and trailing 12 months), stock price (high/low) and 200 or more other factors that are tabulated for each company. Other related and similar data exist for bonds and mutual funds.

Each of these entity types, as well as each type of stock, bond or mutual fund, may exist in one or more indexes, such as bond indexes, stock indexes and mutual fund indexes. Many of these indexes also are tabulated, and have trading vehicles on the American Stock Exchange, the New York Stock Exchange, or NASDAQ. Many of these entities, such as stocks, bonds, mutual funds and indices, are part of or related to an industry segment. These industry segments have related indexes **4122** and trading vehicles as well.

A particular company sells bonds, sells stocks, creates earnings and is part of mutual funds which also creates earnings, dividends and/or interest. Options (securities derivatives of the above instruments) may be impacted by or tightly related to the underlying securities and react accordingly.

Accordingly, an ontology can be created from the above securities data types **4120**, and integration or association of ontologies that can result in the creation of an ontology network according to some embodiments of the present invention. These ontologies may be filled with a great deal of information and relationships, and can be tabulated and stored.

Still referring to Figure 19, an entity-relationship model related to personal data **4110** may relate to an individual. In particular, a capital gains entity **4111**

identifies capital gains in an individual's portfolio, and a portfolio entity **4112** can include a securities balance and a database of personal preferences.

As also shown in Figure 41, a related entity in at least two of the entity-relationship models is identified. In particular, in Figure 19, the stock index entity **4121** and industry index entity **4122** in the securities data entity-relationship model **4120** are related to the economic indicators entity **4137** of the government data entity-relationship model **4130**. Also, the option entity **4143** is related to the corporate bond entity **4127** and mutual fund shares entity **4126**. Finally, the capital gains entity **4111** in the personal data entity-relationship model **4110** is related to the mutual fund share entity **4126** and corporate bond entity **4127** of the securities data entity-relationship model **4120**. Thus, at least some of the related entities that are identified are linked, to thereby create an entity-relationship model that integrates the plurality of databases.

A more detailed description of how the integrated entity-relationship model of Figure 41 may be used by an individual to make portfolio position modifications now will be described. In particular, as also shown in Figure 41, a path rule may be identified that may link the economic indicators entity **4132** and the portfolio entity **4112** using the relationship path rule **4150** that is shown by bold linking arrows in Figure 41.

As the economic indicators **4137** change, they can have an effect, by directly impacting the federal discount rate via Federal Reserve Board action, and/or by impacting the perceived federal discount rate futures **4140**. This economic data and/or federal action, will impact the CBOE options of TNX and TYX **4143**, which are options on the ten year and thirty year Treasury bond rate, and are based on the yield to maturity of the most recently auctioned respective treasury bond. Changes in the value of these instruments are widely watched, and the movement or change in its value can impact the current market, both positively and negatively regarding the sale of corporate bonds **4127**. These instruments may change the current yield **4129**, and/or may result in further change in value as changes occur in the options market for government securities. Bond fund shares **4125** may also change in value and may further sustain changes in current yield, and/or impact value and cause changes in the interest rates assigned to new issues. Finally, these changes can directly result in a capital gain/loss **4111** from the purchase or sale of these equities. This can impact a portfolio database entity **4112**, that includes information on personal preferences of a

customer, and an adjustment or rebalancing of a customer portfolio can be recommended.

The above example shows that there can be relationships to a portfolio balance **4112** that can reside not merely in the databases directly associated with the securities data **4120**, but that can reach further into information warehouses that are removed from the databases relating to the relevant securities data **4120**. This example can be expanded to capture knowledge from those expert in the field that can delineate some or many of the complex relationships that can exist between actions or activities in a global sense that may have a perceived relationship to a portfolio balance, while being remote and/or indirect in a parent/child relationship.

Accordingly, ontology networks, according to some embodiments of the present invention, can be applied to the investment community. In the investment community, investment firms and brokerage houses hire associates to act as portfolio managers or customer client managers. They may have little expert knowledge with regard to the relationships and actions that might indirectly or directly impact particular instruments. Commodity contracts or related security derivatives are examples of such instruments that may be impacted by many peripheral activities or actions that can occur. These actions can include economic, environmental and any other activity, action, event or data that in some way can be related by a combination of traversals to the file, commodity or derivative in question. There presently appears to be a significant need in the securities industry to capture the expert knowledge of the highly experienced investors/traders who may derive their strategies and plans from what could be represented in an ontology network as traversals and association of relationships between key indicators, databases, events, actions and their expected impact on companies and related securities. Embodiments of the invention can allow this expert knowledge to be captured and exploited.

Figure 42 is a more detailed example of an entity-relationship model that integrates a plurality of databases according to some embodiments of the present invention. In Figure 42, relationship types also are indicated. This entity-relationship model may be used to obtain expert advice as to the advisability of a major purchase **4210** based on the integration of government data, securities data and personal data. Accordingly, an ontology network that comprises relationships between securities data from companies and information and relationships contained within a number of government databanks, can be used to create a valuable tool to capture expert

knowledge in this area for use and application by less skilled industry participants and/or by individuals.

Finally, it will be understood that Figures 40-42 provided examples of the integration of personal data, securities data and government data into an ontology network. However, ontology networks may be created in many other fields. Several examples now will be generally described in the fields of criminology/law enforcement, a government budget and the weather. Many other examples may be envisioned by those having skill in the art.

In the field of criminology and law enforcement, data repositories may exist that store retained fingerprint and comparative matching algorithms, DNA data and large databases of information on individuals, where this information on individuals has been generated through either elicit (criminal) activity and/or benign activities, such as public employment. Moreover, local, national and international databases are being developed which include crime scene information and characteristic observations of various crimes. These different ontologies can be merged into an ontology network that could be used, for example, by a task force or other activity whose aim is to understand the nature of organized criminal activity, by integrating the data repositories that are developed on organized crime activities with a host of specific local crime scene information. The relationships that can be established between organized crime activities, national fingerprint databanks, and local crime scene data repositories, can provide an ontology network that can provide new insight into the activities of a criminal organization and/or a clearer focus on their objectives.

In the field of government budgets, it is known that the development of public policy and budgeting for local and national purposes represents a fine balance between the application of funds to various activities relative to public opinion or policies. Accordingly, a relationship may exist between funds that may be available for public welfare, or the creation of new programs, such as a nationally-supported drug subscription plan, and criminal activity on a local, national or international scale. An ontology network, according to some embodiments of the present invention, that integrates international, national and/or local budgetary information and law enforcement data, can be used to provide a predictable understanding of relevant opinion, the results of which may impact other seemingly unrelated programs. This ontology network could be extended to national security, since related data being acquired, as well as the expenses that are entailed, may have an impact on other

totally unrelated expenses, and may also have an impact on public opinion and the resulting policy.

As a final example, an ontology network that uses weather data according to some embodiments of the present invention now will be described. In particular, documentation of world weather patterns can enable the prediction of the character and depth of droughts and heavy rain activity. Other global patterns may be observed with regard to development and progress of storms. These data repositories are being accumulated at significant cost worldwide, and include details and analysis of global data, including data relating to the characteristics of a single storm or weather event, as well as generalizations and characteristics of weather events as types. It is further known that weather events can impact crop yields, with the resulting expectations of profits and losses resulting in impacts to certain related futures trading that may also be occurring on global futures markets. Futures trading and changes in the value of futures contracts can impact the resulting decisions by farmers as to their expectations for profit and planting decisions for the next season. While this may directly impact the general food supply, the futures activities may also impact decisions by farm equipment manufacturers to manufacture farm equipment, which is turn can impact raw materials costs and future buying patterns of commercial buyers in industries related to these material acquisitions. An ontology network according to some embodiments of the present invention can merge ontologies related to weather, crops data, futures trading, farm equipment manufacturing and raw materials. This ontology network then can be traversed by an expert, to establish a path rule for retention of the expert knowledge. Thus, expert thinking can be captured to create a representation that can clearly identify the impact of weather on the cost of steel for increased farm equipment production in the coming year, as an example.

In the drawings and specification, there have been disclosed typical preferred embodiments of the invention and, although specific terms are employed, they are used in a generic and descriptive sense only and not for purposes of limitation, the scope of the invention being set forth in the following claims.

What is Claimed is:

1. A method of integrating a plurality of biological/chemical databases, comprising:

obtaining an entity-relationship model for each of the plurality of biological/chemical databases;

identifying related entities in the entity-relationship models of at least two of the biological/chemical databases; and

linking at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases.

2. A method according to Claim 1 wherein at least one of the plurality of databases represents an ontology and wherein the entity-relationship model that integrates the plurality of biological/chemical databases creates an ontology network.

3. A method according to Claim 1 wherein the related entities are identical entities and wherein linking comprises merging the at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases.

4. A method according to Claim 3 wherein the merging further comprises establishing a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical databases, a respective alias of which refers to a respective one of the at least two of the identical entities that are identified.

5. A method according to Claim 1 further comprising:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

6. A method according to Claim 5 wherein the traversing comprises:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases from a starting entity to an ending entity in response to a query that specifies the starting entity and the ending entity to thereby identify relationships between the starting entity and the ending entity that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

7. A method according to Claim 5 wherein the traversing comprises:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

8. A method according to Claim 5 wherein the traversing comprises:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query and in response to at least one path rule to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

9. A method according to Claim 8 wherein the at least one path rule specifies a type of path to use in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type of path not to use in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type of ending entity that can be included in the query results, a type of ending entity that is not to be included in the query results, a type or class of relationship to be used in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type or class of relationship that is not to be used in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases and/or a confidence level to be achieved in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases.

10. A method according to Claim 8 further comprising storing the query and the path rule for reuse.

11. A method according to Claim 5 further comprising:

storing the query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases.

12. A method according to Claim 5 further comprising:

assigning a confidence level to at least one of the relationships in the entity-relationship model that integrates the plurality of biological/chemical databases.

13. A method according to Claim 12 further comprising:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases including the at least one confidence level that is assigned.

14. A method of integrating a new biological/chemical database with a plurality of biological/chemical databases, comprising:

providing an entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in at least two of the biological/chemical databases;

obtaining an entity-relationship model of the new biological/chemical database;

identifying related entities in the entity-relationship model of the new biological/chemical database and the entity-relationship model of the plurality of biological/chemical databases; and

linking at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

15. A method according to Claim 14 wherein the entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in the at least two of the biological/chemical databases provides an ontology network and wherein the entity-relationship model for the new biological/chemical database represents an ontology.

16. A method according to Claim 14 wherein the related entities are identical entities and wherein the linking comprises merging the at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

17. A method according to Claim 16 wherein the merging further comprises establishing a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database, a respective alias of which refers to a respective one of the at last two of the identical entities that are identified.

18. A method according to Claim 17 wherein the new biological/chemical database is an updated version of one of the plurality of biological/chemical databases, the method further comprising:

identifying at least one entity in the one of the plurality of biological/chemical databases that has been deleted from the updated version of the one of the plurality of biological/chemical databases; and

removing an alias that is associated with the at least one entity that has been removed.

19. A method according to Claim 18 further comprising:

splitting at least one entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database based upon the alias that was removed.

20. A method according to Claim 14 further comprising:

identifying entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database; and

adding at least one new entity to the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database that corresponds to the entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

21. A method according to Claim 14 further comprising:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

22. A method according to Claim 14 further comprising:

traversing the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database in response to a query and in response to at least one path rule to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

23. A method according to Claim 21 further comprising:

storing the query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database as at least one new relationship in the entity-relationship

model that integrates the plurality of biological/chemical databases and the new biological/chemical database to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

24. A method according to Claim 14 further comprising:

maintaining an image of the entity-relationship model of the plurality of biological/chemical databases prior to the linking.

25. A method according to Claim 24 further comprising:

comparing the image of the entity-relationship model of the plurality of biological/chemical databases prior to the linking and the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

26. A method according to Claim 14 wherein the entity-relationship model of the new biological/chemical database does not include relationships therein.

27. A method of querying a plurality of biological/chemical databases, each of which includes records for a plurality of biological/chemical entities, the method comprising:

providing an integrated entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in at least two of the biological/chemical databases; and

traversing the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

28. A method according to Claim 27 wherein the traversing comprises:

traversing the integrated entity-relationship model of the plurality of biological/chemical databases from a starting entity to an ending entity in response to a query that specifies the starting entity and the ending entity to thereby identify

relationships between the starting entity and the ending entity that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

29. A method according to Claim 27 wherein the traversing comprises:

traversing the integrated entity-relationship model of the plurality of biological/chemical databases from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

30. A method according to Claim 27 wherein the traversing comprises:

traversing the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query and in response to at least one path rule to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

31. A method according to Claim 30 wherein the at least one path rule specifies a type of path to use in traversing through the plurality of entities, a type of path not to use in traversing through the plurality of entities, a type of ending entity that can be included in the query results, a type or class of ending entity that is not to be included in the query results, a type or class of relationship that is to be used in traversing through the plurality of entities, a type of relationship not to be used in traversing through the plurality of entities and/or a confidence level to be achieved in traversing through the plurality of entities.

32. A method according to Claim 30 further comprising storing the query and the path rule for reuse.

33. A method according to Claim 27 further comprising:

storing the query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases as at least one new relationship in the integrated entity-relationship model of the plurality of biological/chemical databases to thereby store knowledge that was derived from the

query in the integrated entity-relationship model of the plurality of biological/chemical databases.

34. A method according to Claim 27 further comprising:

assigning a confidence level to at least one of the relationships in the integrated entity-relationship model of the plurality of biological/chemical databases.

35. A method according to Claim 34 further comprising:

traversing the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases including the at least one confidence level that is assigned.

36. A system for integrating a plurality of biological/chemical databases, comprising:

an entity-relationship model for each of the plurality of biological/chemical databases;

means for identifying related entities in the entity-relationship models of at least two of the biological/chemical databases; and

means for linking at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases.

37. A system according to Claim 36 wherein at least one of the plurality of databases represents an ontology and wherein the entity-relationship model that integrates the plurality of biological/chemical databases creates an ontology network.

38. A system according to Claim 36 wherein the related entities are identical entities and wherein the means for linking comprises means for merging the at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases.

39. A system according to Claim 38 wherein the means for merging further comprises means for establishing a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical databases, a respective alias of which refers to a respective one of the at least two of the identical entities that are identified.

40. A system according to Claim 36 further comprising:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

41. A system according to Claim 40 wherein the means for traversing comprises:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases from a starting entity to an ending entity in response to a query that specifies the starting entity and the ending entity to thereby identify relationships between the starting entity and the ending entity that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

42. A system according to Claim 40 wherein the means for traversing comprises:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

43. A system according to Claim 40 wherein the means for traversing comprises:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query and in response to at least one

path rule to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

44. A system according to Claim 43 wherein the at least one path rule specifies a type of path to use in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type of path not to use in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type of ending entity that can be included in the query results, a type of ending entity that is not to be included in the query results, a type or class of relationship to be used in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type or class of relationship that is not to be used in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases and/or a confidence level to be achieved in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases.

45. A system according to Claim 43 further comprising means for storing the query and the path rule for reuse.

46. A system according to Claim 40 further comprising:

means for storing the query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases.

47. A system according to Claim 40 further comprising:

means for assigning a confidence level to at least one of the relationships in the entity-relationship model that integrates the plurality of biological/chemical databases.

48. A system according to Claim 47 further comprising:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases including the at least one confidence level that is assigned.

49. A system for integrating a new biological/chemical database with a plurality of biological/chemical databases, comprising:

an entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in at least two of the biological/chemical databases;

an entity-relationship model of the new biological/chemical database;

means for identifying related entities in the entity-relationship model of the new biological/chemical database and the entity-relationship model of the plurality of biological/chemical databases; and

means for linking at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

50. A system according to Claim 49 wherein the entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in the at least two of the biological/chemical databases provides an ontology network and wherein the entity-relationship model for the new biological/chemical database represents an ontology.

51. A system according to Claim 49 wherein the related entities are identical entities and wherein the means for linking comprises means for merging the at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

52. A system according to Claim 51 wherein the means for merging further comprises means for establishing a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical

databases and the new biological/chemical database, a respective alias of which refers to a respective one of the at last two of the identical entities that are identified.

53. A system according to Claim 52 wherein the new biological/chemical database is an updated version of one of the plurality of biological/chemical databases, the system further comprising:

means for identifying at least one entity in the one of the plurality of biological/chemical databases that has been deleted from the updated version of the one of the plurality of biological/chemical databases; and

means for removing an alias that is associated with the at least one entity that has been removed.

54. A system according to Claim 53 further comprising:

means for splitting at least one entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database based upon the alias that was removed.

55. A system according to Claim 49 further comprising:

means for identifying entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database; and

means for adding at least one new entity to the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database that corresponds to the entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

56. A system according to Claim 49 further comprising:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database in response to a query to thereby obtain query results that are based on the entity-

relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

57. A system according to Claim 49 further comprising:

means for traversing the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database in response to a query and in response to at least one path rule to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

58. A system according to Claim 56 further comprising:

means for storing the query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

59. A system according to Claim 49 further comprising:

means for maintaining an image of the entity-relationship model of the plurality of biological/chemical databases before the at least two of the related entities are linked.

60. A system according to Claim 54 further comprising:

means for comparing the image of the entity-relationship model of the plurality of biological/chemical databases before the at least two of the related entities are linked and the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

61. A system according to Claim 49 wherein the entity-relationship model of the new biological/chemical database does not include relationships therein.

62. A system for querying a plurality of biological/chemical databases, each of which includes records for a plurality of biological/chemical entities, the system comprising:

an integrated entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in at least two of the biological/chemical databases; and

means for traversing the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

63. A system according to Claim 62 wherein the means for traversing comprises:

means for traversing the integrated entity-relationship model of the plurality of biological/chemical databases from a starting entity to an ending entity in response to a query that specifies the starting entity and the ending entity to thereby identify relationships between the starting entity and the ending entity that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

64. A system according to Claim 62 wherein the means for traversing comprises:

means for traversing the integrated entity-relationship model of the plurality of biological/chemical databases from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

65. A system according to Claim 62 wherein the means for traversing comprises:

means for traversing the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query and in response to at least one path rule to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

66. A system according to Claim 65 wherein the at least one path rule specifies a type of path to use in traversing through the plurality of entities, a type of path not to use in traversing through the plurality of entities, a type of ending entity that can be included in the query results, a type of ending entity that is not to be included in the query results, a type or class of relationship that is to be used in traversing through the plurality of entities, a type or class of relationship not to be used in traversing through the plurality of entities and/or a confidence level to be achieved in traversing through the plurality of entities.

67. A system according to Claim 65 further comprising storing the query and the path rule for reuse.

68. A system according to Claim 62 further comprising:

means for storing the query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases as at least one new relationship in the integrated entity-relationship model of the plurality of biological/chemical databases to thereby store knowledge that was derived from the query in the integrated entity-relationship model of the plurality of biological/chemical databases.

69. A system according to Claim 62 further comprising:

means for assigning a confidence level to at least one of the relationships in the integrated entity-relationship model of the plurality of biological/chemical databases.

70. A system according to Claim 69 further comprising:

means for traversing the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases including the at least one confidence level that is assigned.

71. A computer program product that is configured to integrate a plurality of biological/chemical databases, the computer program product comprising a

computer usable storage medium having computer-readable program code embodied in the medium, the computer-readable program code comprising:

computer-readable program code that is configured to obtain an entity-relationship model for each of the plurality of biological/chemical databases;

computer-readable program code that is configured to identify related entities in the entity-relationship models of at least two of the biological/chemical databases; and

computer-readable program code that is configured to link at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases.

72. A computer program product according to Claim 71 wherein at least one of the plurality of databases represents an ontology and wherein the entity-relationship model that integrates the plurality of biological/chemical databases creates an ontology network.

73. A computer program product according to Claim 71 wherein the related entities are identical entities and wherein the computer-readable program code that is configured to link comprises computer-readable program code that is configured to merge the at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases.

74. A computer program product according to Claim 73 wherein the computer-readable program code that is configured to merge further comprises computer-readable program code that is configured to establish a plurality of aliases for the single entity in the entity-relationship model that integrates the plurality of biological/chemical databases, a respective alias of which refers to a respective one of the at least two of the identical entities that are identified.

75. A computer program product according to Claim 71 further comprising:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases in

response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

76. A computer program product according to Claim 75 wherein the computer-readable program code that is configured to traverse comprises:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases from a starting entity to an ending entity in response to a query that specifies the starting entity and the ending entity to thereby identify relationships between the starting entity and the ending entity that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

77. A computer program product according to Claim 75 wherein the computer-readable program code that is configured to traverse comprises:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

78. A computer program product according to Claim 75 wherein the computer-readable program code that is configured to traverse comprises:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query and in response to at least one path rule to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases.

79. A computer program product according to Claim 78 wherein the at least one path rule specifies a type of path to use in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type of path not to use in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type of ending entity that

can be included in the query results, a type of ending entity that is not to be included in the query results, a type or class of relationship to be used in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases, a type or class of relationship that is not to be used in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases and/or a confidence level to be achieved in traversing through the entity-relationship model that integrates the plurality of biological/chemical databases.

80. A computer program product according to Claim 78 further comprising computer-readable program code that is configured to store the query and the path rule for reuse.

81. A computer program product according to Claim 75 further comprising:

computer-readable program code that is configured to store the query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases.

82. A computer program product according to Claim 75 further comprising:

computer-readable program code that is configured to assign a confidence level to at least one of the relationships in the entity-relationship model that integrates the plurality of biological/chemical databases.

83. A computer program product according to Claim 82 further comprising:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases including the at least one confidence level that is assigned.

84. A computer program product that is configured to integrate a new biological/chemical database with a plurality of biological/chemical databases, the computer program product comprising a computer usable storage medium having computer-readable program code embodied in the medium, the computer-readable program code comprising:

an entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in at least two of the biological/chemical databases;

an entity-relationship model of the new biological/chemical database;

computer-readable program code that is configured to identify related entities in the entity-relationship model of the new biological/chemical database and the entity-relationship model of the plurality of biological/chemical databases; and

computer-readable program code that is configured to link at least two of the related entities that are identified, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

85. A computer program product according to Claim 84 wherein the entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in the at least two of the biological/chemical databases provides an ontology network and wherein the entity-relationship model for the new biological/chemical database represents an ontology.

86. A computer program product according to Claim 84 wherein the related entities are identical entities and wherein the computer-readable program code that is configured to link comprises computer-readable program code that is configured to merge the at least two of the identical entities that are identified into a single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

87. A computer program product according to Claim 86 wherein the computer-readable program code that is configured to merge further comprises computer-readable program code that is configured to establish a plurality of aliases

for the single entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database, a respective alias of which refers to a respective one of the at last two of the identical entities that are identified.

88. A computer program product according to Claim 87 wherein the new biological/chemical database is an updated version of one of the plurality of biological/chemical databases, the computer program product further comprising:

computer-readable program code that is configured to identify at least one entity in the one of the plurality of biological/chemical databases that has been deleted from the updated version of the one of the plurality of biological/chemical databases; and

computer-readable program code that is configured to remove an alias that is associated with the at least one entity that has been removed.

89. A computer program product according to Claim 88 further comprising:

computer-readable program code that is configured to split at least one entity in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database based upon the alias that was removed.

90. A computer program product according to Claim 84 further comprising:

computer-readable program code that is configured to identify entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database; and

computer-readable program code that is configured to add at least one new entity to the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database that corresponds to the entities in the new biological/chemical database that do not correspond to at least one of the entities in the entity-relationship model that

integrates the plurality of biological/chemical databases and the new biological/chemical database.

91. A computer program product according to Claim 84 further comprising:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database in response to a query to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

92. A computer program product according to Claim 84 further comprising:

computer-readable program code that is configured to traverse the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database in response to a query and in response to at least one path rule to thereby obtain query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

93. A computer program product according to Claim 91 further comprising:

computer-readable program code that is configured to store the query results that are based on the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases and the new biological/chemical database.

94. A computer program products according to Claim 84 further comprising:

computer-readable program code that is configured to maintain an image of the entity-relationship model of the plurality of biological/chemical databases before the at least two of the related entities are linked.

95. A computer program product according to Claim 94 further comprising:

computer-readable program code that is configured to compare the image of the entity-relationship model of the plurality of biological/chemical databases before the at least two of the related entities are linked and the entity relationship mode that integrates the plurality of biological chemical databases and the new biological/chemical database.

96. A computer program product according to Claim 84 wherein the entity-relationship model of the new biological/chemical database does not include relationships therein.

97. A computer program product that is configured to query a plurality of biological/chemical databases, each of which includes records for a plurality of biological/chemical entities, the computer program product comprising a computer usable storage medium having computer-readable program code embodied in the medium, the computer-readable program code comprising:

an integrated entity-relationship model of the plurality of biological/chemical databases that links at least some related entities in at least two of the biological/chemical databases; and

computer-readable program code that is configured to traverse the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

98. A computer program product according to Claim 97 wherein the computer-readable program code that is configured to traverse comprises:

computer-readable program code that is configured to traverse the integrated entity-relationship model of the plurality of biological/chemical databases from a starting entity to an ending entity in response to a query that specifies the starting

entity and the ending entity to thereby identify relationships between the starting entity and the ending entity that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

99. A computer program product according to Claim 97 wherein the computer-readable program code that is configured to traverse comprises:

computer-readable program code that is configured to traverse the integrated entity-relationship model of the plurality of biological/chemical databases from a starting entity to a plurality of ending entities in response to a query that specifies the starting entity to thereby identify relationships between the starting entity and the plurality of ending entities that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

100. A computer program product according to Claim 97 wherein the computer-readable program code that is configured to traverse comprises:

computer-readable program code that is configured to traverse the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query and in response to at least one path rule to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases.

101. A computer program product according to Claim 100 wherein the at least one path rule specifies a type of path to use in traversing through the plurality of entities, a type of path not to use in traversing through the plurality of entities, a type of ending entity that can be included in the query results, a type of ending entity that is not to be included in the query results, a type or class of relationship that is to be used in traversing through the plurality of entities, a type or class of relationship not to be used in traversing through the plurality of entities and/or a confidence level to be achieved in traversing through the plurality of entities.

102. A computer program products according to Claim 100 further comprising computer-readable program code that is configured to store the query and the path rule for reuse.

103. A computer program product according to Claim 97 further comprising:

computer-readable program code that is configured to store the query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases as at least one new relationship in the integrated entity-relationship model of the plurality of biological/chemical databases to thereby store knowledge that was derived from the query in the integrated entity-relationship model of the plurality of biological/chemical databases.

104. A computer program product according to Claim 97 further comprising:

computer-readable program code that is configured to assign a confidence level to at least one of the relationships in the integrated entity-relationship model of the plurality of biological/chemical databases.

105. A computer program product according to Claim 104 further comprising:

computer-readable program code that is configured to traverse the integrated entity-relationship model of the plurality of biological/chemical databases in response to a query to thereby obtain query results that are based on the integrated entity-relationship model of the plurality of biological/chemical databases including the at least one confidence level that is assigned.

106. A bioinformatics data processing system comprising:

an ontology network engine that is configured to build an integrated entity-relationship model of a plurality of independent biological/chemical databases, each of which includes records for a plurality of biological/chemical objects, the integrated entity-relationship model comprising:

a plurality of entities, a respective one of which corresponds to a single biological/chemical object, at least some of the entities including a plurality of links, a respective one of which directly or indirectly refers to at least one record in a respective one of the plurality of biological/chemical databases that relates to the single biological/chemical object; and

a plurality of relationships that link the plurality of entities in the entity-relationship model based upon relationships therebetween.

107. A system according to Claim 106 further comprising:

a metadata database that is configured to store therein the integrated entity-relationship model of the plurality of independent biological/chemical databases.

108. A system according to Claim 106 further comprising:

a loader that is configured to load an independent entity-relationship model of each of the independent biological/chemical databases into the ontology network engine.

109. A system according to Claim 108 wherein the loader is configured to load an independent entity-relationship model of each of the independent biological/chemical databases into the ontology network engine in a typeless format.

110. A system according to Claim 108 in combination with the plurality of independent biological/chemical databases.

111. A system according to Claim 106 further comprising:

a query tool that is configured to traverse the integrated entity-relationship model in response to a query to thereby obtain query results that are based on the integrated entity-relationship model.

112. A system according to Claim 111 wherein the query tool is a Web-based query tool.

113. A system according to Claim 106 further comprising:

a virtual experiment tool that is configured to conduct virtual experiments on the integrated entity-relationship model.

114. A system according to Claim 106 further comprising:

a discovery tool that is configured to discover biological/chemical knowledge from the integrated entity-relationship model.

115. A system according to Claim 106 wherein the ontology network engine runs on a plurality of data processing systems that are configured in a peer-to-peer configuration.

116. A bioinformatics data structure comprising:

an integrated entity-relationship model of a plurality of independent biological/chemical databases, each of which includes records for a plurality of biological/chemical objects, the integrated entity-relationship model comprising:

a plurality of entities, a respective entity of which corresponds to a single biological/chemical object, at least some of the entities including a plurality of links, a respective one of which directly or indirectly refers to at least one record in a respective one of the plurality of biological/chemical databases that relates to the single biological/chemical object; and

a plurality of relationships that link the plurality of entities in the entity-relationship model based upon relationships therebetween.

117. A data structure according to Claim 116 further comprising:

an independent entity-relationship model of each of the independent biological/chemical databases.

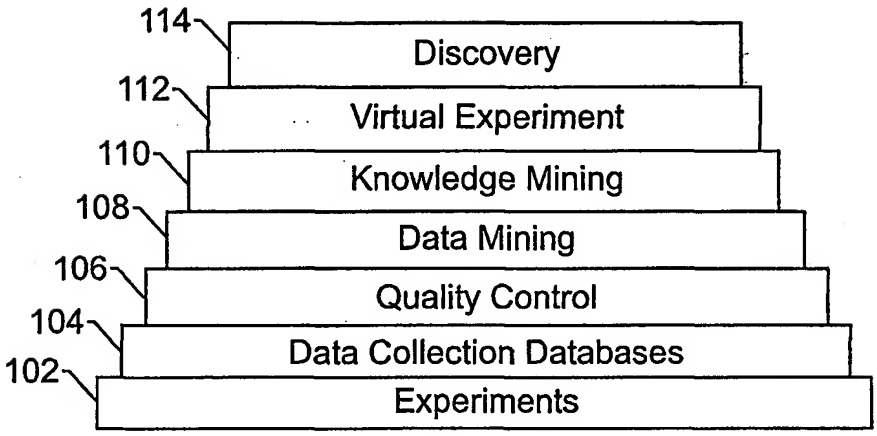

114
Discovery
112
Virtual Experiment
110
Knowledge Mining
108
Data Mining
106
Quality Control
104
Data Collection Databases
102
Experiments

FIG. 1.

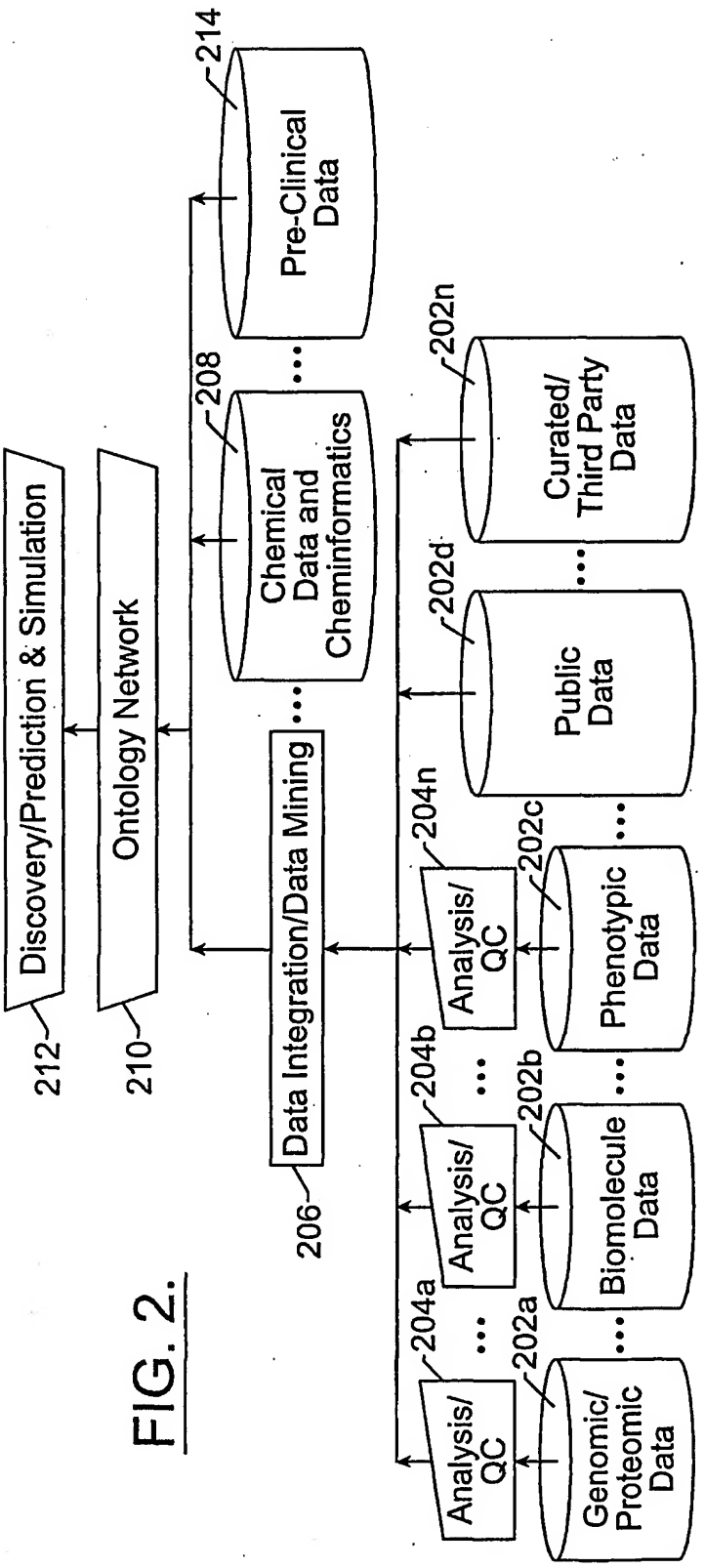

Discovery/Prediction & Simulation
Ontology Network
Data Integration/Data Mining
Chemical Data and Cheminformatics
Pre-Clinical Data
Curated/ Third Party Data
Public Data
Phenotypic Data
Biomolecule Data
Genomic/ Proteomic Data
Analysis/ QC
212
210
206
208
214
202n
202d
202c
202b
202a
204n
204b
204a

FIG. 2.

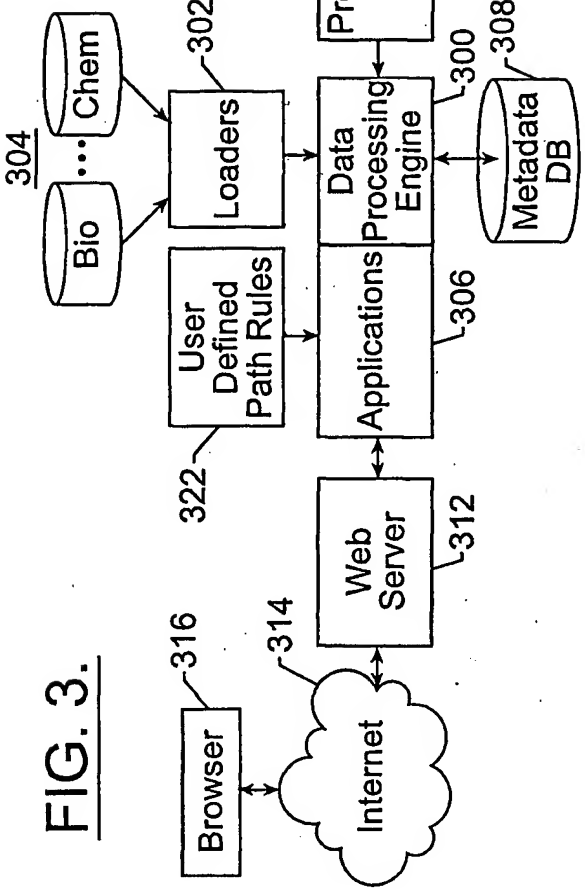

304
Bio
Chem
Loaders
302
User Defined Path Rules
322
Predefined Path Rules
324
Data Processing Engine
300
Metadata DB
308
Applications
306
Web Server
312
Internet
314
Browser
316

FIG. 3.

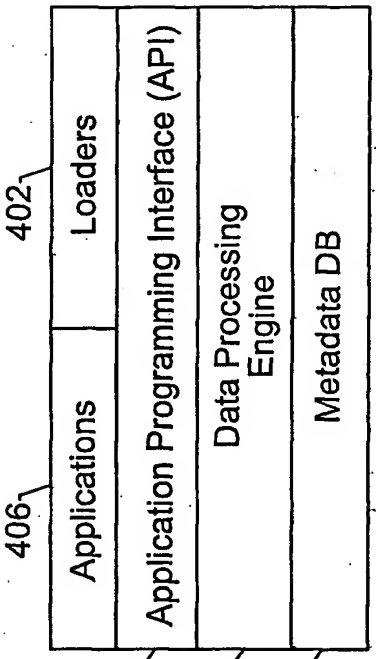

402
Loaders
406
Applications
Application Programming Interface (API)
Data Processing Engine
Metadata DB
430
400
408

FIG. 4.

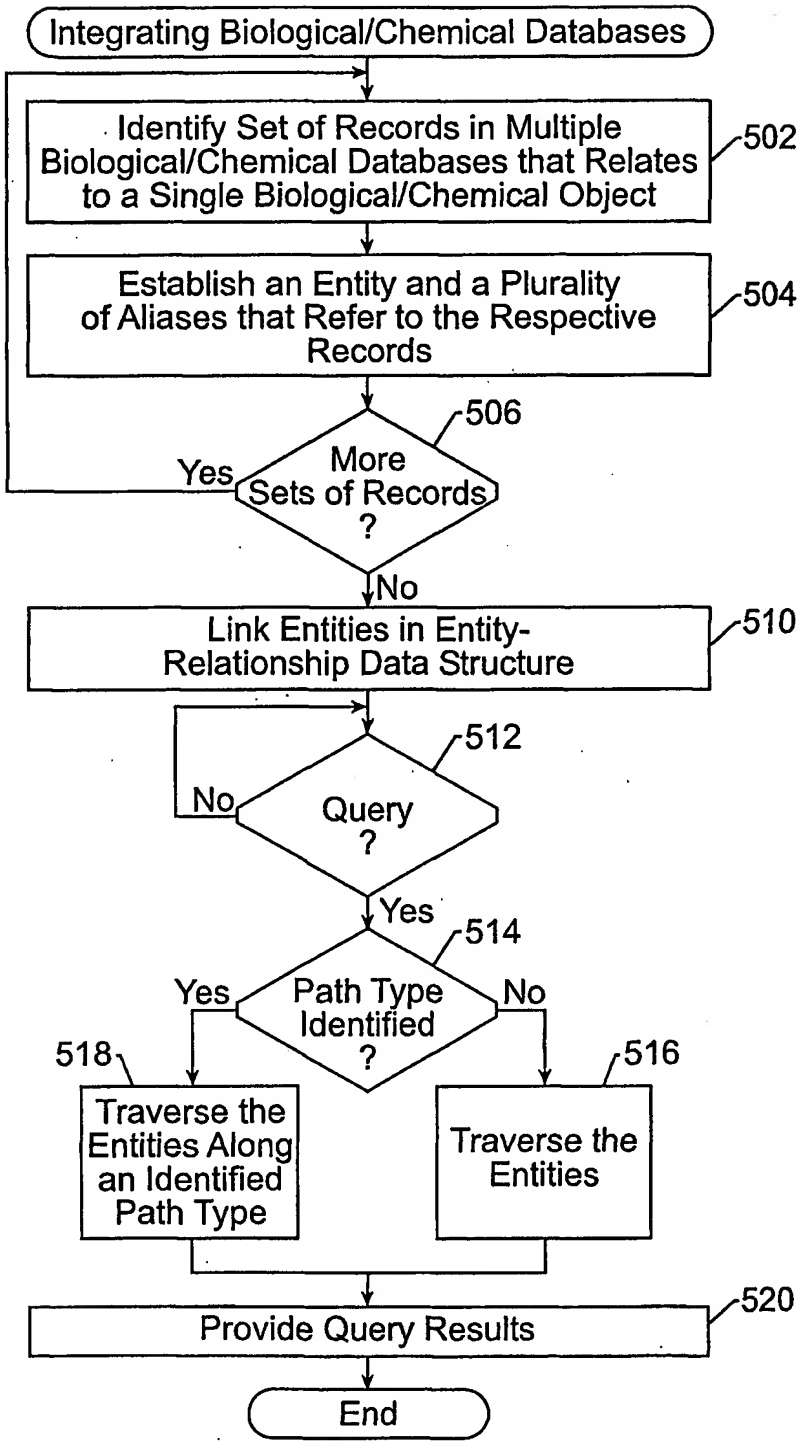

Integrating Biological/Chemical Databases
Identify Set of Records in Multiple Biological/Chemical Databases that Relates to a Single Biological/Chemical Object
502
Establish an Entity and a Plurality of Aliases that Refer to the Respective Records
504
506
More Sets of Records ?
Yes
No
Link Entities in Entity-Relationship Data Structure
510
512
Query ?
No
Yes
514
Path Type Identified ?
Yes
No
518
516
Traverse the Entities Along an Identified Path Type
Traverse the Entities
Provide Query Results
520
End

FIG. 5.

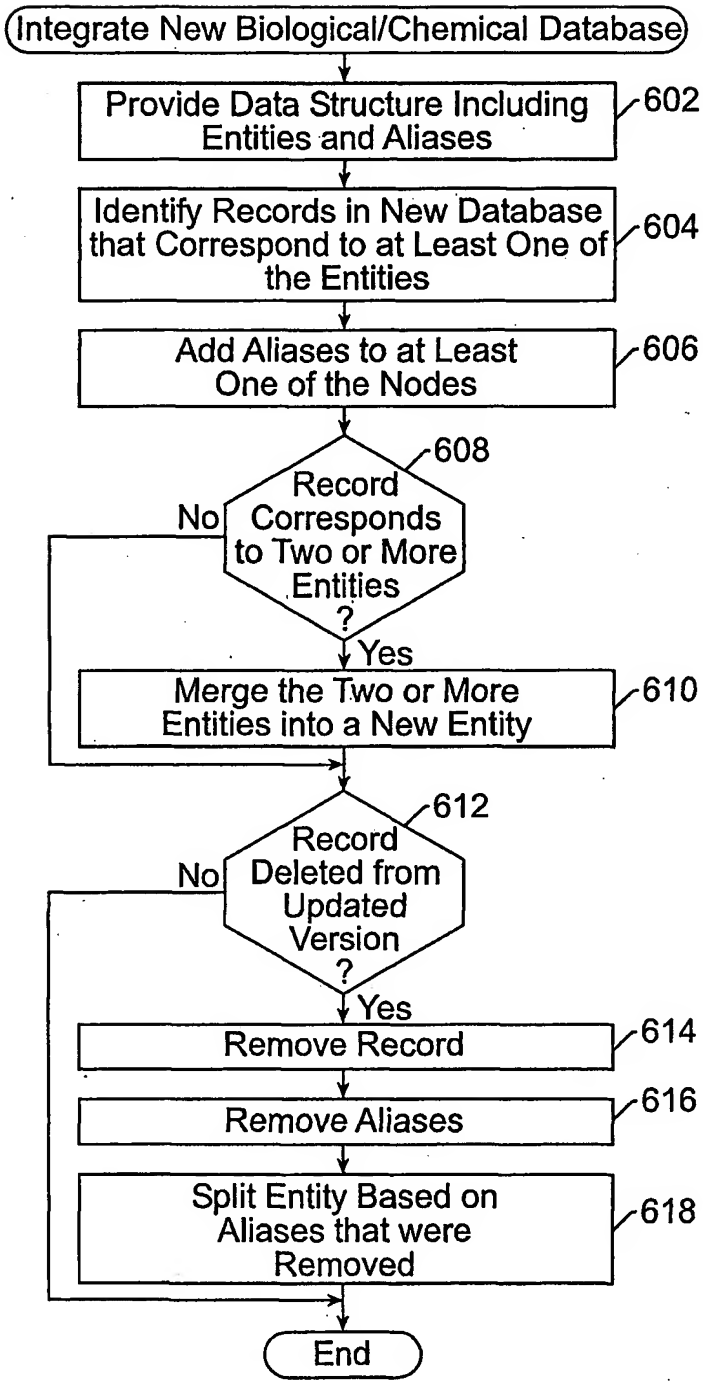

Integrate New Biological/Chemical Database
Provide Data Structure Including Entities and Aliases
602
Identify Records in New Database that Correspond to at Least One of the Entities
604
Add Aliases to at Least One of the Nodes
606
608
Record Corresponds to Two or More Entities ?
No
Yes
Merge the Two or More Entities into a New Entity
610
612
Record Deleted from Updated Version ?
No
Yes
Remove Record
614
Remove Aliases
616
Split Entity Based on Aliases that were Removed
618
End

FIG. 6.

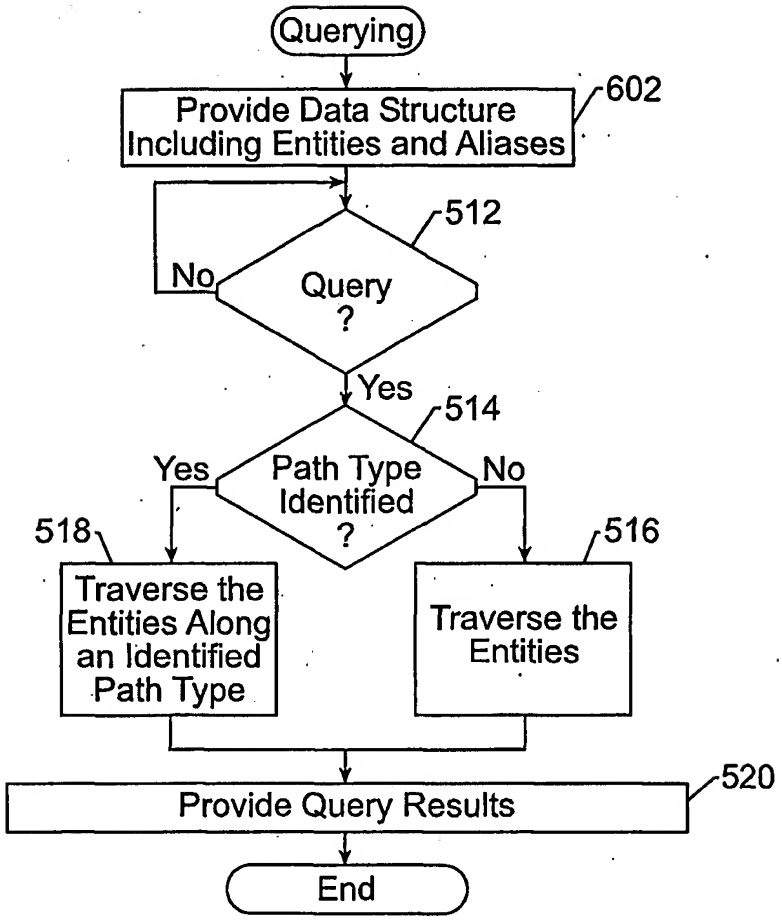

Querying
Provide Data Structure Including Entities and Aliases
602
512
No
Query ?
Yes
514
Yes
Path Type Identified ?
No
518
516
Traverse the Entities Along an Identified Path Type
Traverse the Entities
520
Provide Query Results
End

FIG. 7.

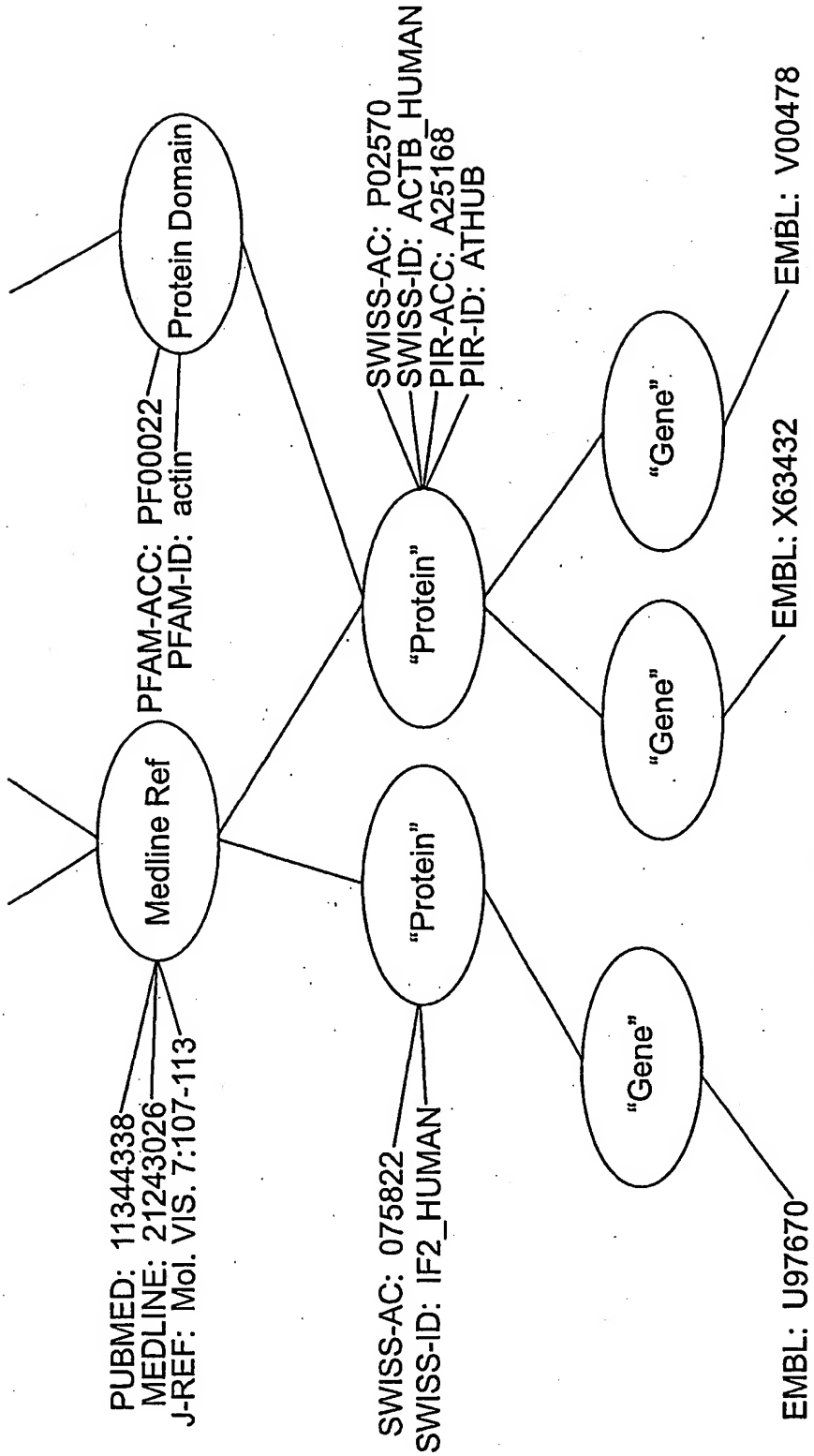

Protein Domain
PFAM-ACC: PF00022
PFAM-ID: actin
Medline Ref
PUBMED: 11344338
MEDLINE: 21243026
J-REF: Mol. VIS. 7:107-113
"Protein"
SWISS-AC: P02570
SWISS-ID: ACTB_HUMAN
PIR-ACC: A25168
PIR-ID: ATHUB
"Protein"
SWISS-AC: 075822
SWISS-ID: IF2_HUMAN
"Gene"
EMBL: V00478
"Gene"
EMBL: X63432
"Gene"
EMBL: U97670

FIG. 8.

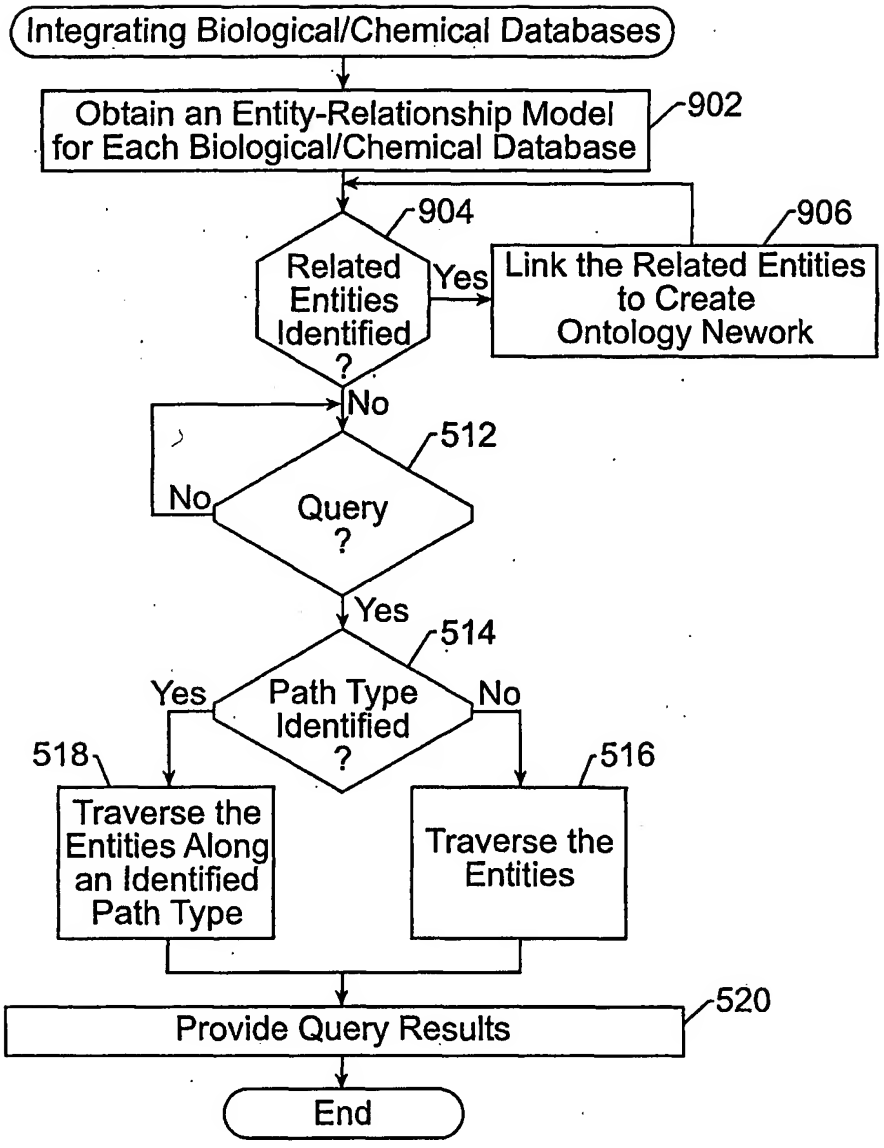

Integrating Biological/Chemical Databases
Obtain an Entity-Relationship Model for Each Biological/Chemical Database
902
904
Related Entities Identified ?
Yes
906
Link the Related Entities to Create Ontology Nework
No
512
No
Query ?
Yes
514
Yes
Path Type Identified ?
No
518
516
Traverse the Entities Along an Identified Path Type
Traverse the Entities
Provide Query Results
520
End

FIG. 9.

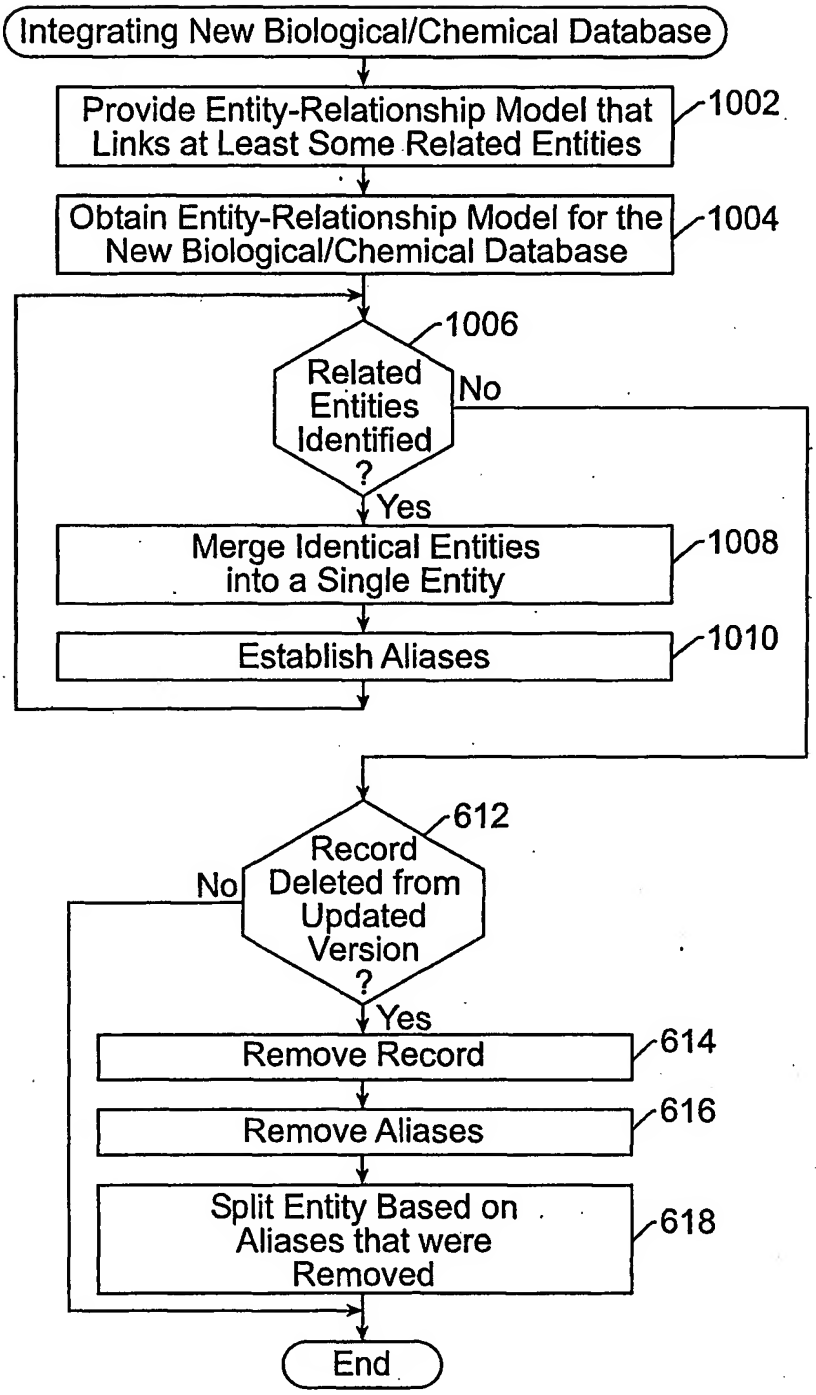

Integrating New Biological/Chemical Database
Provide Entity-Relationship Model that Links at Least Some Related Entities
1002
Obtain Entity-Relationship Model for the New Biological/Chemical Database
1004
1006
Related Entities Identified ?
No
Yes
Merge Identical Entities into a Single Entity
1008
Establish Aliases
1010
612
Record Deleted from Updated Version ?
No
Yes
Remove Record
614
Remove Aliases
616
Split Entity Based on Aliases that were Removed
618
End

FIG. 10.

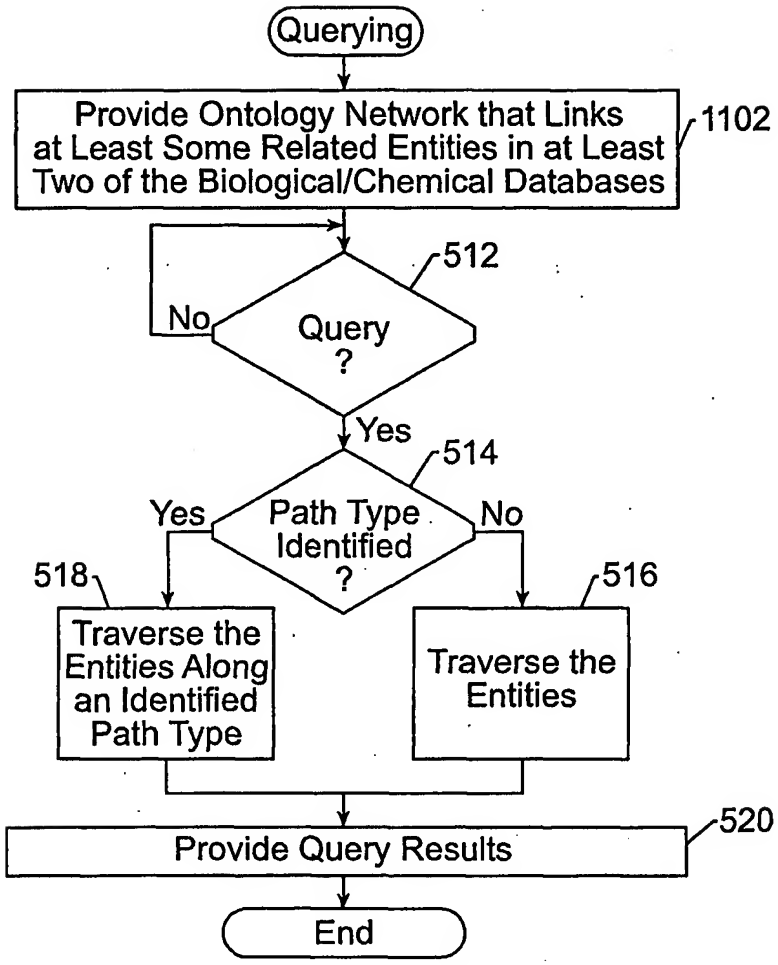

Querying
Provide Ontology Network that Links at Least Some Related Entities in at Least Two of the Biological/Chemical Databases
1102
512
No
Query ?
Yes
514
Yes
Path Type Identified ?
No
518
516
Traverse the Entities Along an Identified Path Type
Traverse the Entities
520
Provide Query Results
End

FIG. 11.

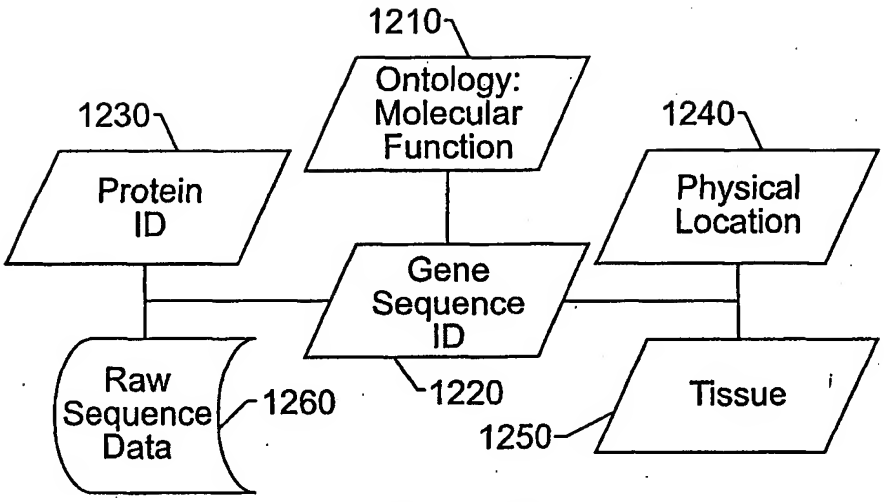

1210
Ontology: Molecular Function
1230
Protein ID
1240
Physical Location
Gene Sequence ID
Raw Sequence Data
1260
1220
Tissue
1250

FIG. 12.

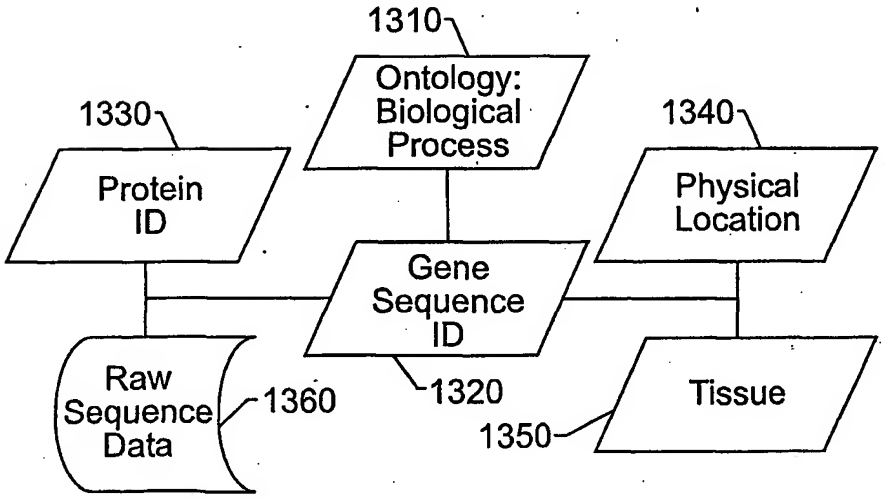

1310
Ontology: Biological Process
1330
Protein ID
1340
Physical Location
Gene Sequence ID
Raw Sequence Data
1360
1320
Tissue
1350

FIG. 13.

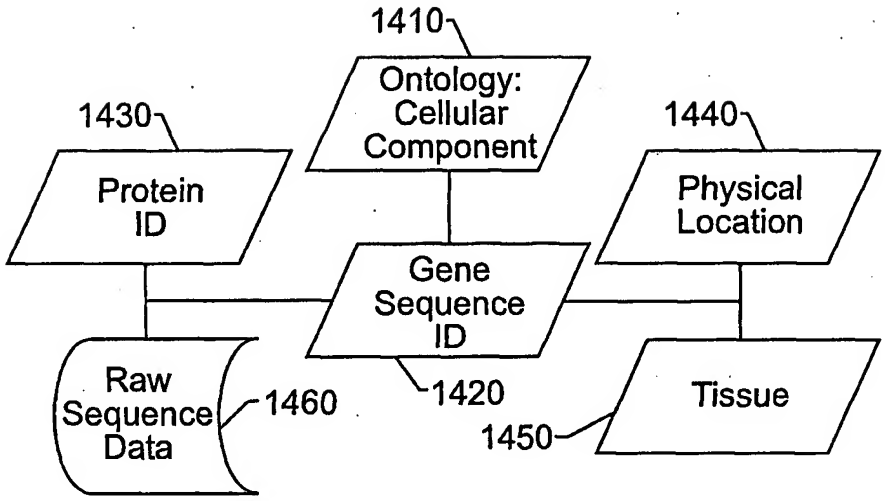

1410
Ontology: Cellular Component
1430
Protein ID
1440
Physical Location
Gene Sequence ID
Raw Sequence Data
1460
1420
Tissue
1450

FIG. 14.

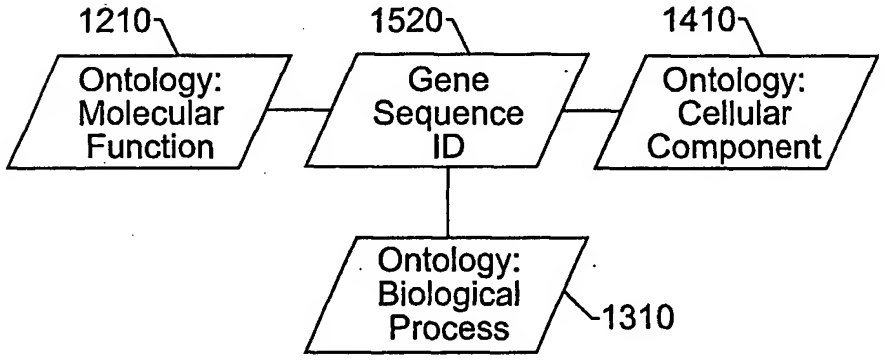

1210
Ontology: Molecular Function
1520
Gene Sequence ID
1410
Ontology: Cellular Component
Ontology: Biological Process
1310

FIG. 15.

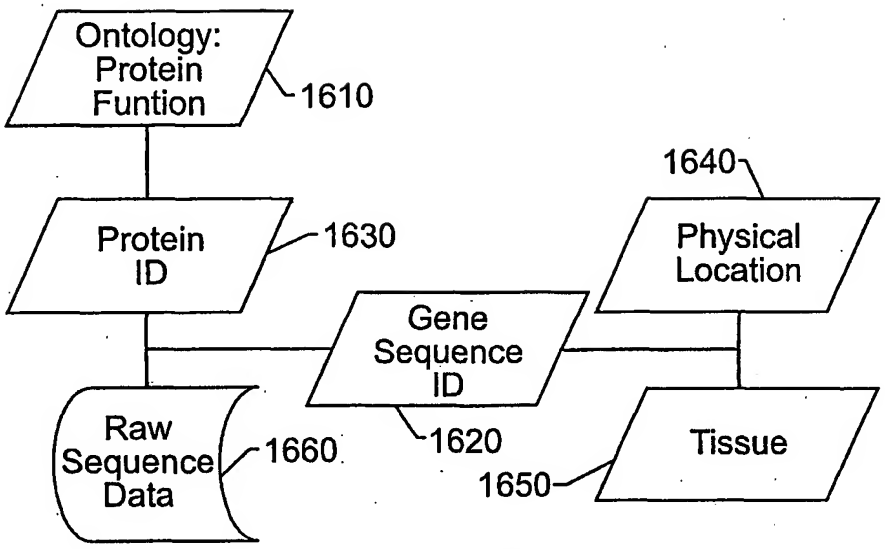

Ontology: Protein Funtion
1610
1640
Protein ID
1630
Physical Location
Gene Sequence ID
Raw Sequence Data
1660
1620
Tissue
1650

FIG. 16.

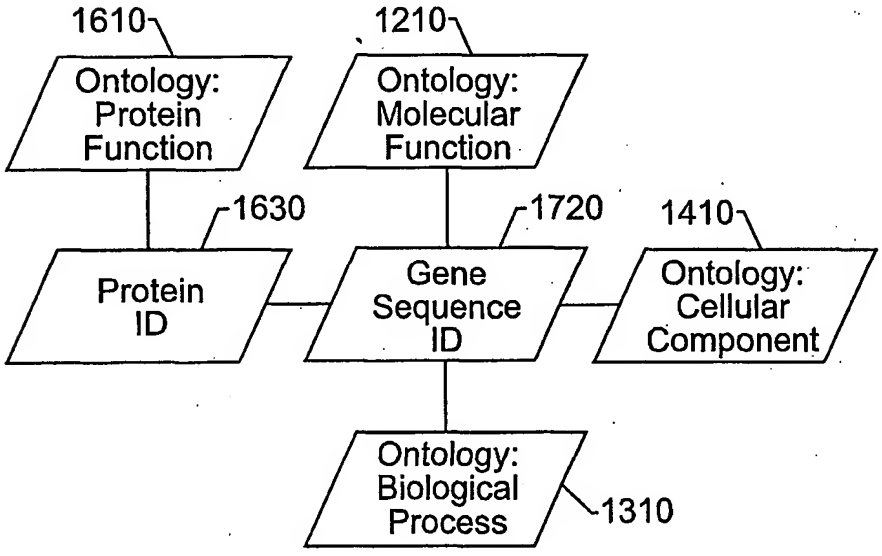

1610
1210
Ontology: Protein Function
Ontology: Molecular Function
1630
1720
1410
Protein ID
Gene Sequence ID
Ontology: Cellular Component
Ontology: Biological Process
1310

FIG. 17.

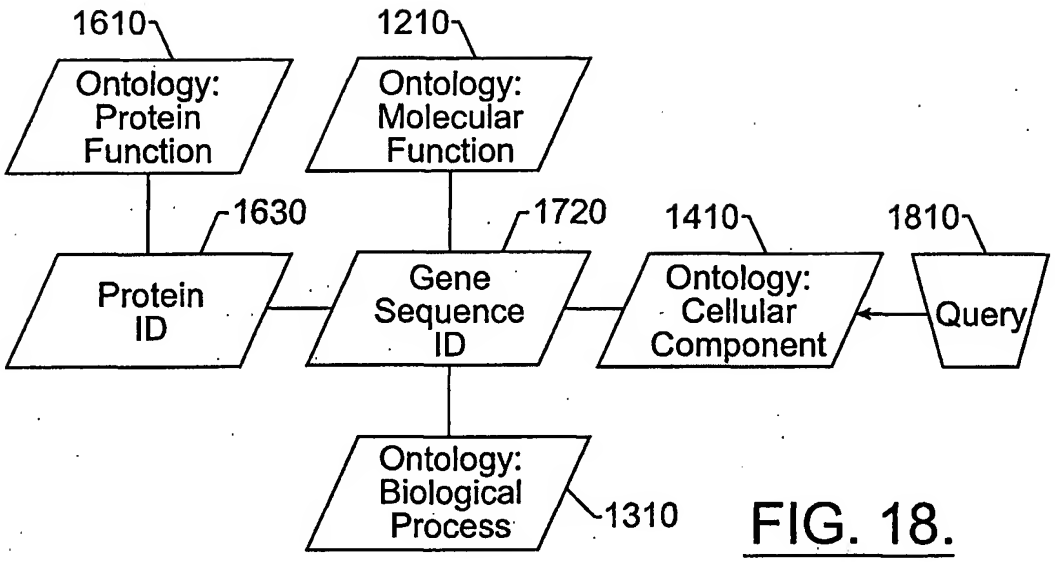

1610
Ontology: Protein Function
1210
Ontology: Molecular Function
1630
Protein ID
1720
Gene Sequence ID
1410
Ontology: Cellular Component
1810
Query
Ontology: Biological Process
1310

FIG. 18.

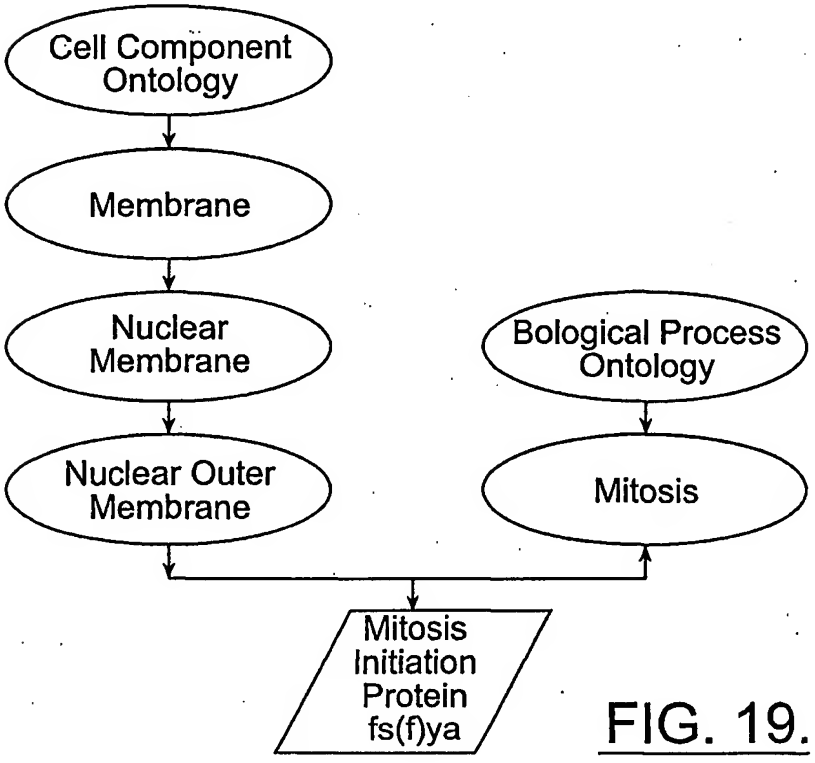

Cell Component Ontology
Membrane
Nuclear Membrane
Nuclear Outer Membrane
Bological Process Ontology
Mitosis
Mitosis Initiation Protein fs(f)ya

FIG. 19.

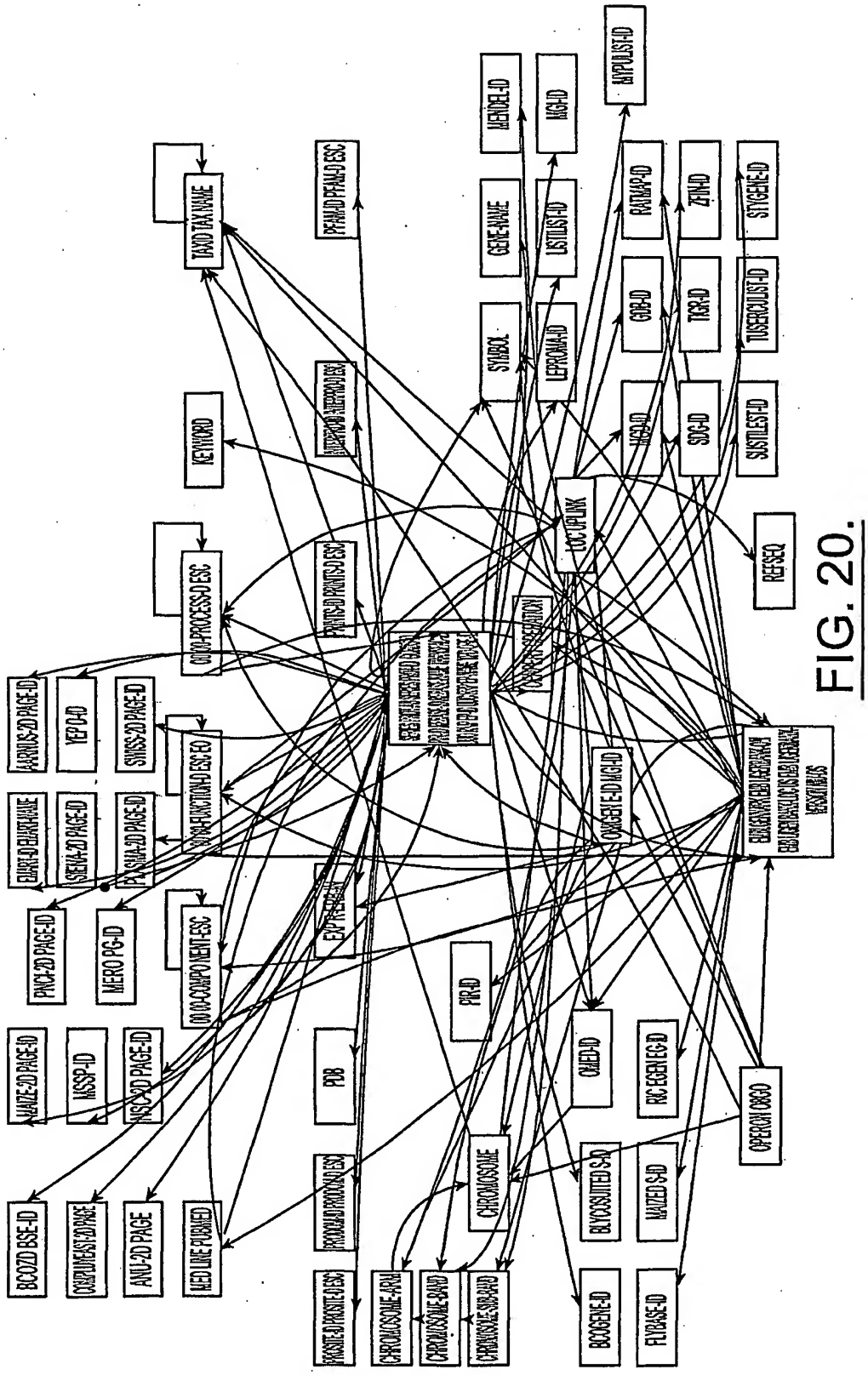

TAXID TAX NAME
KEYWORD
OMIM-PROCESS-ID ESC
PRINTS-ID PRINTS-ID ESC
INTERPRO-ID INTERPRO ESC
PFAM-ID PFAM-ID ESC
MENDEL-ID
MGI-ID
GENE-NAME
LSTILIST-ID
SYMBOL
LEPROMA-ID
AMPLIST-ID
RATMAP-ID
ZFIN-ID
STYGENE-ID
GDB-ID
TIGR-ID
TIGRORGLIST-ID
HGM-ID
SGC-ID
SINSTILEST-ID
LOCUSLINK
REFSEQ
AARNIUS-2D PAGE-ID
YEP I-H-ID
SWISS-2D PAGE-ID
BURFI-ID BURFI NAME
SIENA-2D PAGE-ID
PANA-2D PAGE-ID
PINCI-2D PAGE-ID
MERO PG-ID
MAIZE-2D PAGE-ID
NSSP-ID
NSC-2D PAGE-ID
BCOZD BSE-ID
OSMIUM-ST 2D PAGE
ANU-2D PAGE
MED LINE PUBMED
PDB
PROXIMUS PROXIMUS ESC
TRANSFAC TRANSFAC ID ESC
PIR-ID
EXP REFSEQ
CHROMOSOME-ARM
CHROMOSOME-BAND
CHROMOSOME SUB-BAND
CHROMOSOME
OMED-ID
BIOSUBMITTED S-ID
BCOGENE-ID
RIC EGEN EG-ID
MAIZED S-ID
FLYBASE-ID
OPERON ORGO

FIG. 20.

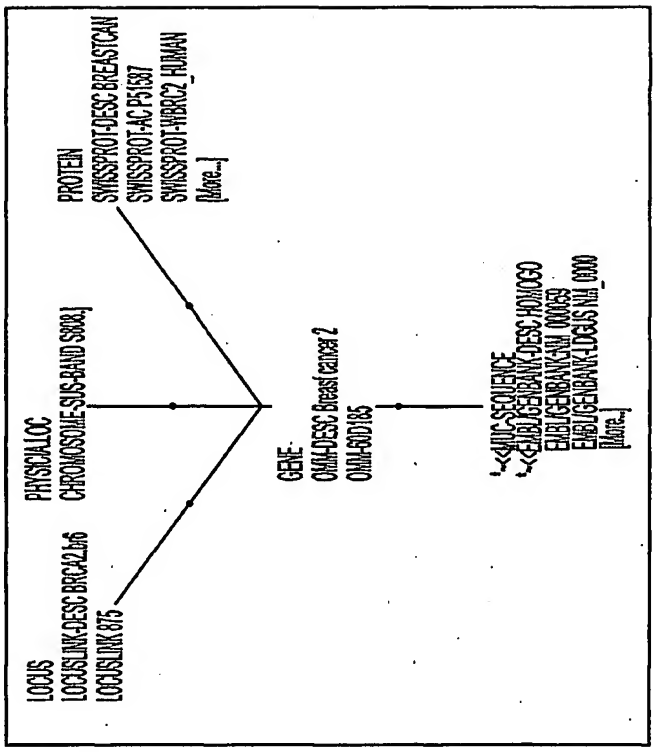
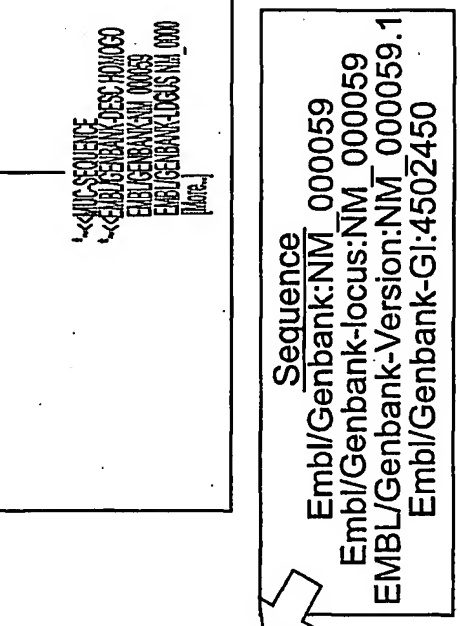
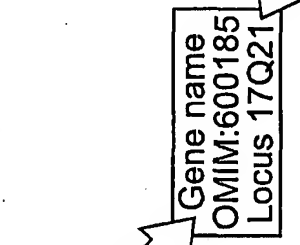
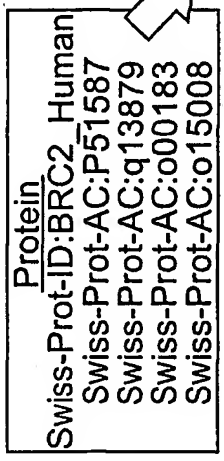

LOCUS
LOCUSLINK:DESC:BRCA2Ab6
LOCUSLINK:875
PHYSICALLOC
CHROMOSOME-SUS-BAND S800;]
PROTEIN
SWISSPROT-DESC:BREASTCAN
SWISSPROT-AC:P51587
SWISSPROT-WBRC2_HUMAN
[More...]
GENE
OMIM-DESC:Breast cancer 2
OMIM-600185
MMC-SEQUENCE
EMBL/GENBANK-DESC:HDMOCO
EMBL/GENBANK-NM_000059
EMBL/GENBANK-LOCUS:NM_0000
[More...]

FIG. 21.


Sequence
Embl/Genbank:NM_000059
Embl/Genbank-locus:NM_000059
EMBL/Genbank-Version:NM_000059.1
Embl/Genbank-GI:4502450


Gene name
OMIM:600185
Locus 17Q21


Protein
Swiss-Prot-ID:BRC2_Human
Swiss-Prot-AC:P51587
Swiss-Prot-AC:q13879
Swiss-Prot-AC:o00183
Swiss-Prot-AC:o15008

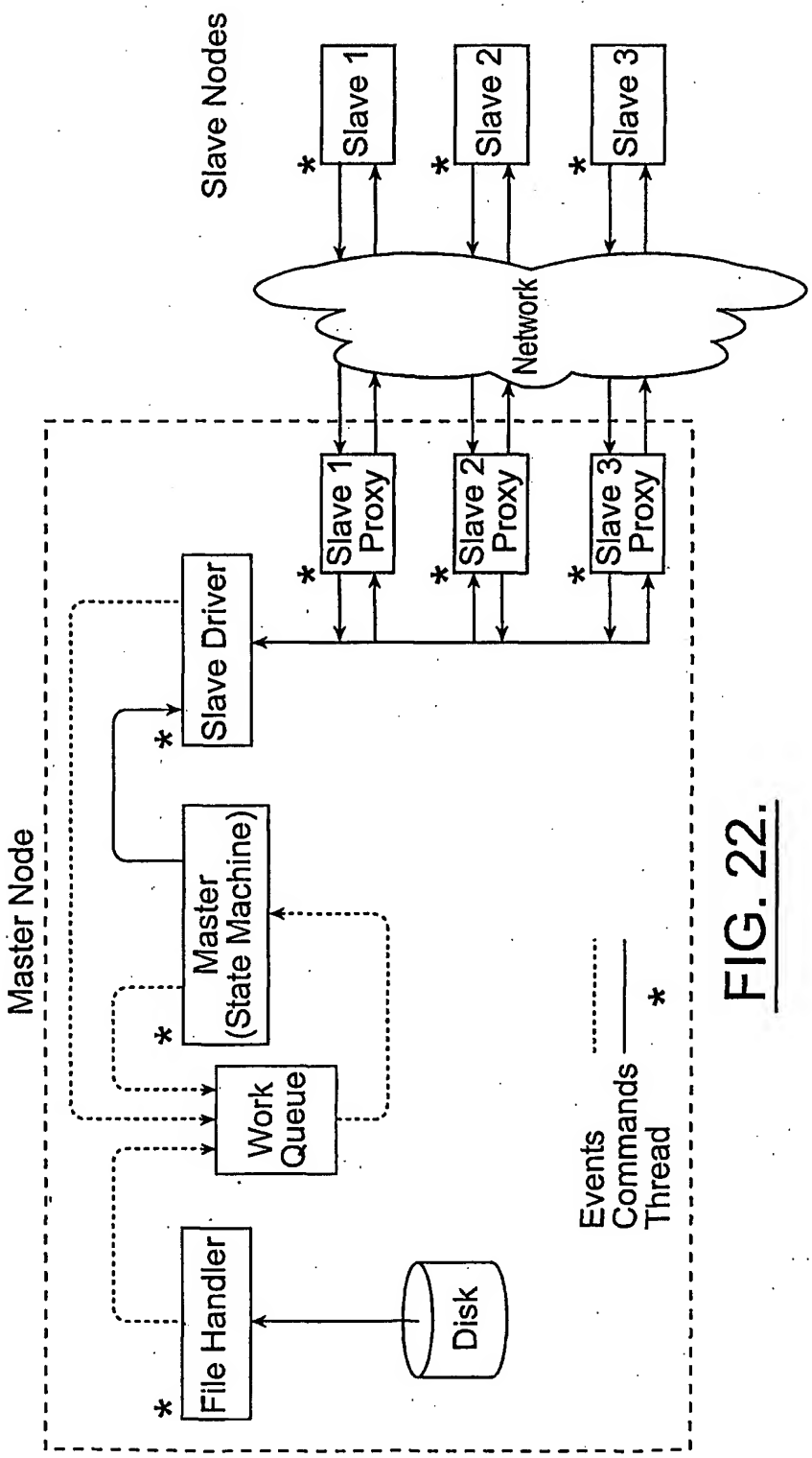

Slave Nodes
Slave 1
Slave 2
Slave 3
Network
Slave 1 Proxy
Slave 2 Proxy
Slave 3 Proxy
Master Node
Slave Driver
Master (State Machine)
Work Queue
File Handler
Disk
Events
Commands
Thread
*

FIG. 22.

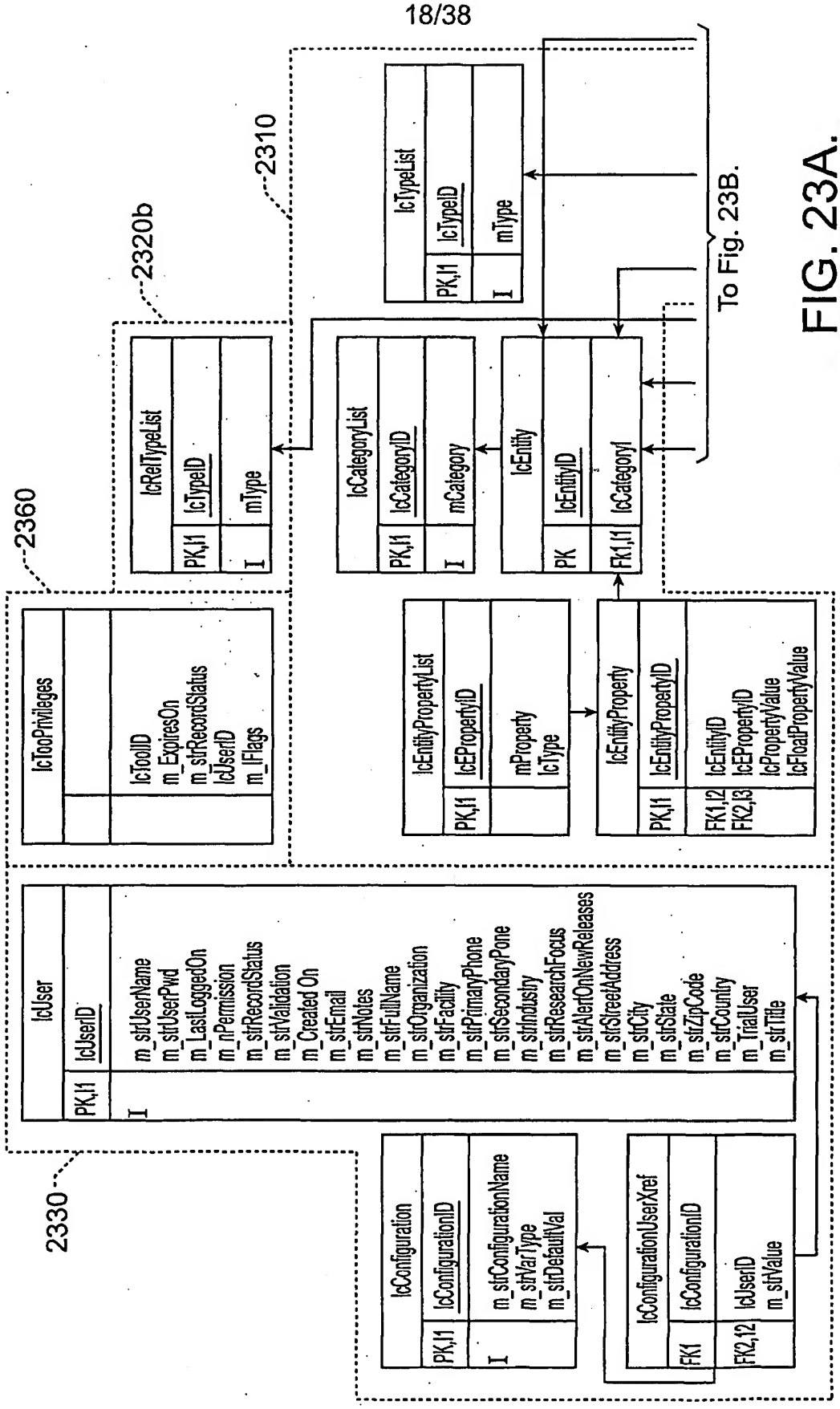

2330
2360
2310
2320b
IcUser
PK,I1
IcUserID
I
m_strUserName
m_strUserPwd
m_LastLoggedOn
m_nPermission
m_strRecordStatus
m_strValidation
m_Created On
m_strEmail
m_strNotes
m_strFullName
m_strOrganization
m_strFacility
m_strPrimaryPhone
m_strSecondaryPone
m_strIndustry
m_strResearchFocus
m_strAlertOnNewReleases
m_strStreetAddress
m_strCity
m_strState
m_strZipCode
m_strCountry
m_TrialUser
m_strTitle
IcConfiguration
PK,I1
IcConfigurationID
I
m_strConfigurationName
m_strVarType
m_strDefaultVal
IcConfigurationUserXref
FK1
IcConfigurationID
FK2,I2
IcUserID
m_strValue
IcToolPrivileges
IcToolID
m_ExpiresOn
m_strRecordStatus
IcUserID
m_lFlags
IcRelTypeList
PK,I1
IcTypeID
I
mType
IcCategoryList
PK,I1
IcCategoryID
I
mCategory
IcEntity
PK
IcEntityID
FK1,I1
IcCategoryI
IcTypeList
PK,I1
IcTypeID
I
mType
IcEntityPropertyList
PK,I1
IcEPropertyID
mProperty
IcType
IcEntityProperty
PK,I1
IcEntityPropertyID
FK1,I2
FK2,I3
IcEntityID
IcEPropertyID
IcPropertyValue
IcFloatPropertyValue
To Fig. 23B.

FIG. 23A.

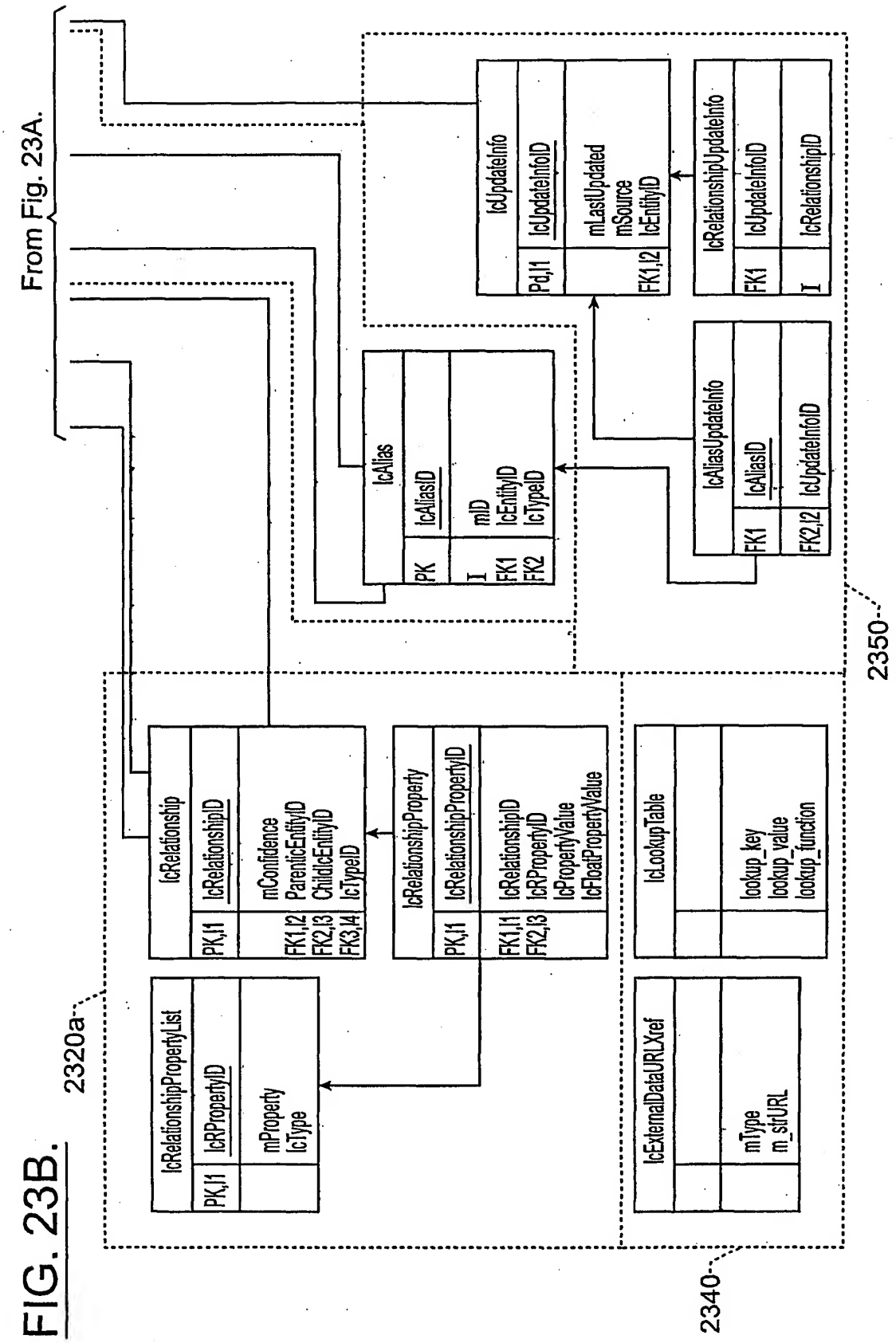

From Fig. 23A.
2320a
2340
2350
IcRelationship
PK,I1
IcRelationshipID
mConfidence
ParenticEntityID
ChildIcEntityID
IcTypeID
FK1,I2
FK2,I3
FK3,I4
IcRelationshipProperty
PK,I1
IcRelationshipPropertyID
IcRelationshipID
IcRPropertyID
IcPropertyValue
IcFloatPropertyValue
FK1,I1
FK2,I3
IcRelationshipPropertyList
PK,I1
IcRPropertyID
mProperty
IcType
IcLookupTable
lookup_key
lookup_value
lookup_function
IcExternalDataURLXref
mType
m_strURL
IcAlias
PK
IcAliasID
I
mID
IcEntityID
IcTypeID
FK1
FK2
IcUpdateInfo
Pd,I1
IcUpdateInfoID
mLastUpdated
mSource
IcEntityID
FK1,I2
IcAliasUpdateInfo
FK1
IcAliasID
FK2,I2
IcUpdateInfoID
IcRelationshipUpdateInfo
FK1
IcUpdateInfoID
I
IcRelationshipID

FIG. 23B.

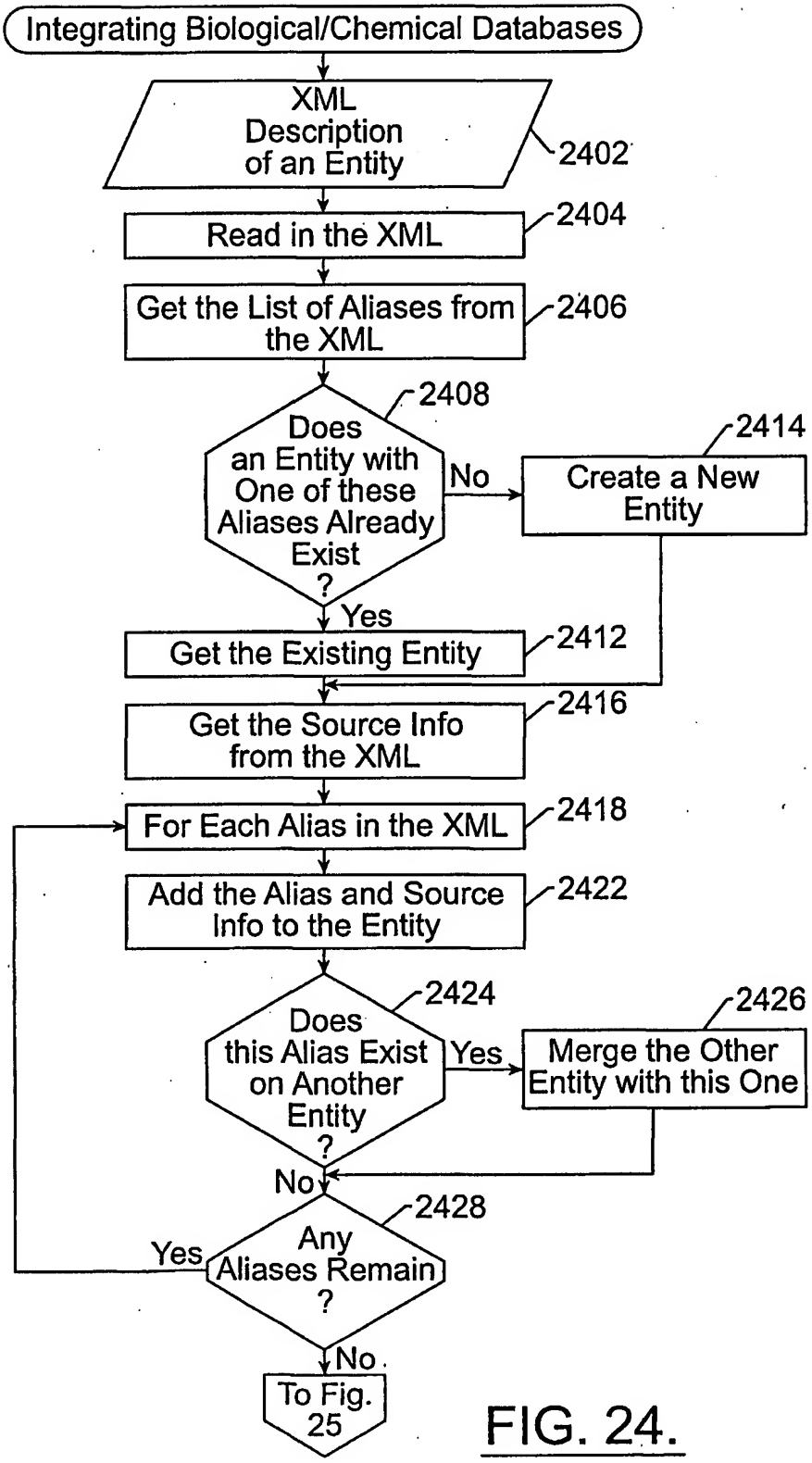

Integrating Biological/Chemical Databases
XML Description of an Entity
2402
Read in the XML
2404
Get the List of Aliases from the XML
2406
2408
Does an Entity with One of these Aliases Already Exist ?
No
2414
Create a New Entity
Yes
Get the Existing Entity
2412
Get the Source Info from the XML
2416
For Each Alias in the XML
2418
Add the Alias and Source Info to the Entity
2422
2424
Does this Alias Exist on Another Entity ?
Yes
2426
Merge the Other Entity with this One
No
2428
Any Aliases Remain ?
Yes
No
To Fig. 25

FIG. 24.

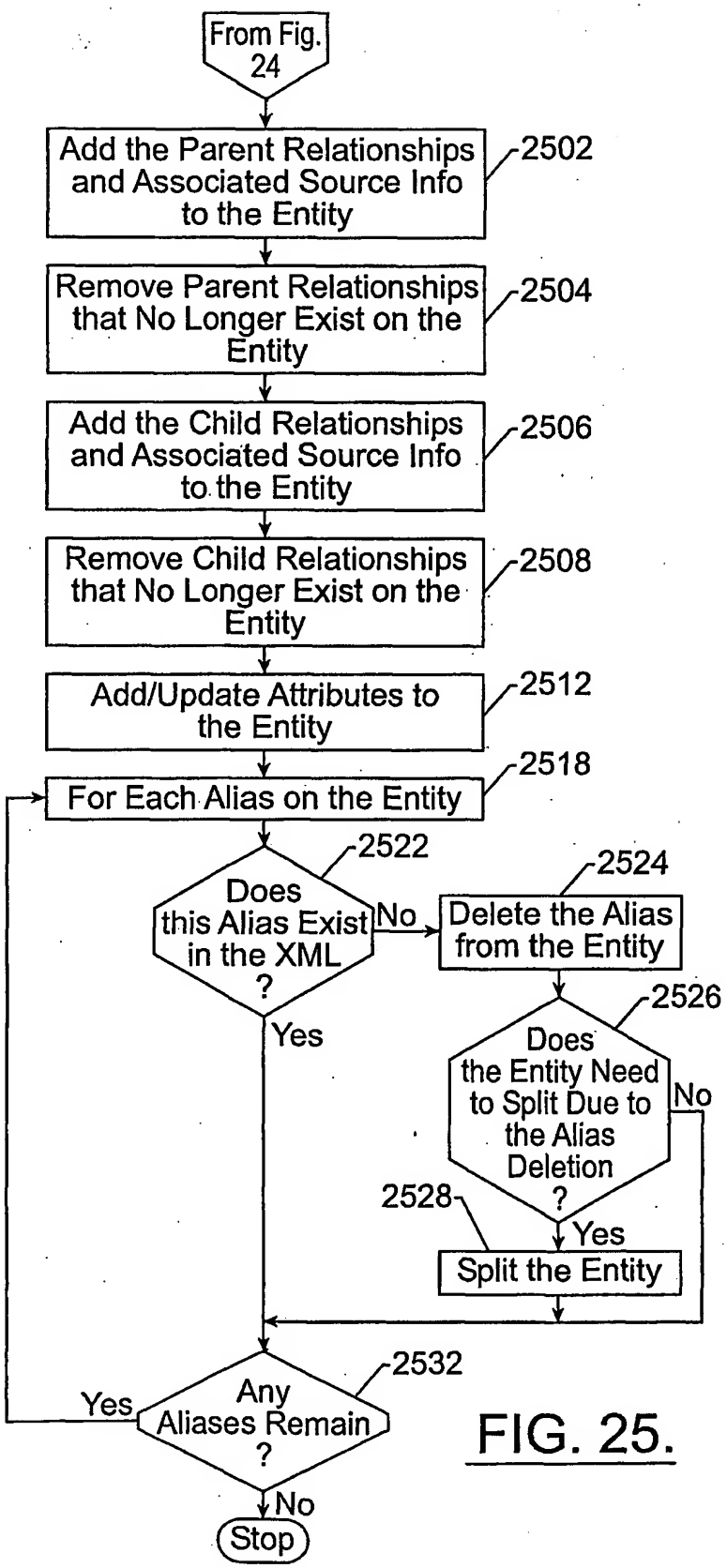

From Fig. 24
Add the Parent Relationships and Associated Source Info to the Entity
2502
Remove Parent Relationships that No Longer Exist on the Entity
2504
Add the Child Relationships and Associated Source Info to the Entity
2506
Remove Child Relationships that No Longer Exist on the Entity
2508
Add/Update Attributes to the Entity
2512
For Each Alias on the Entity
2518
Does this Alias Exist in the XML ?
2522
No
Delete the Alias from the Entity
2524
Yes
Does the Entity Need to Split Due to the Alias Deletion ?
2526
No
Yes
2528
Split the Entity
Any Aliases Remain ?
2532
Yes
No
Stop

FIG. 25.

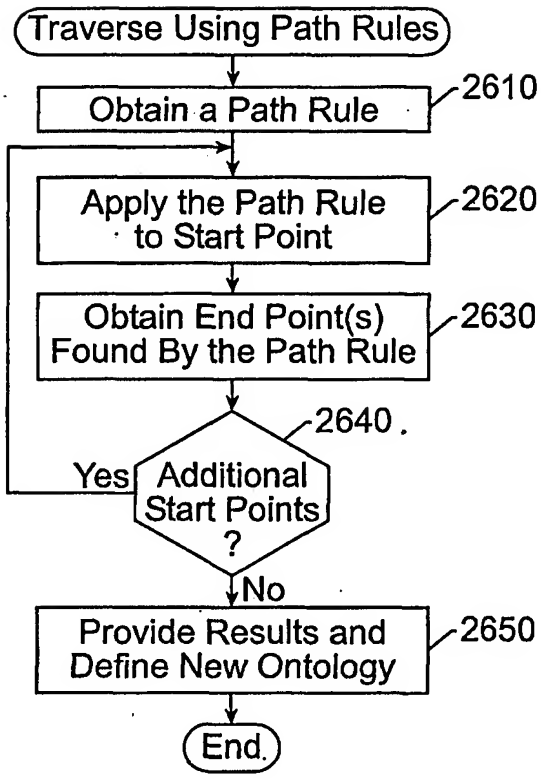

Traverse Using Path Rules
Obtain a Path Rule
2610
Apply the Path Rule to Start Point
2620
Obtain End Point(s) Found By the Path Rule
2630
2640
Yes
Additional Start Points ?
No
Provide Results and Define New Ontology
2650
End.

FIG. 26.

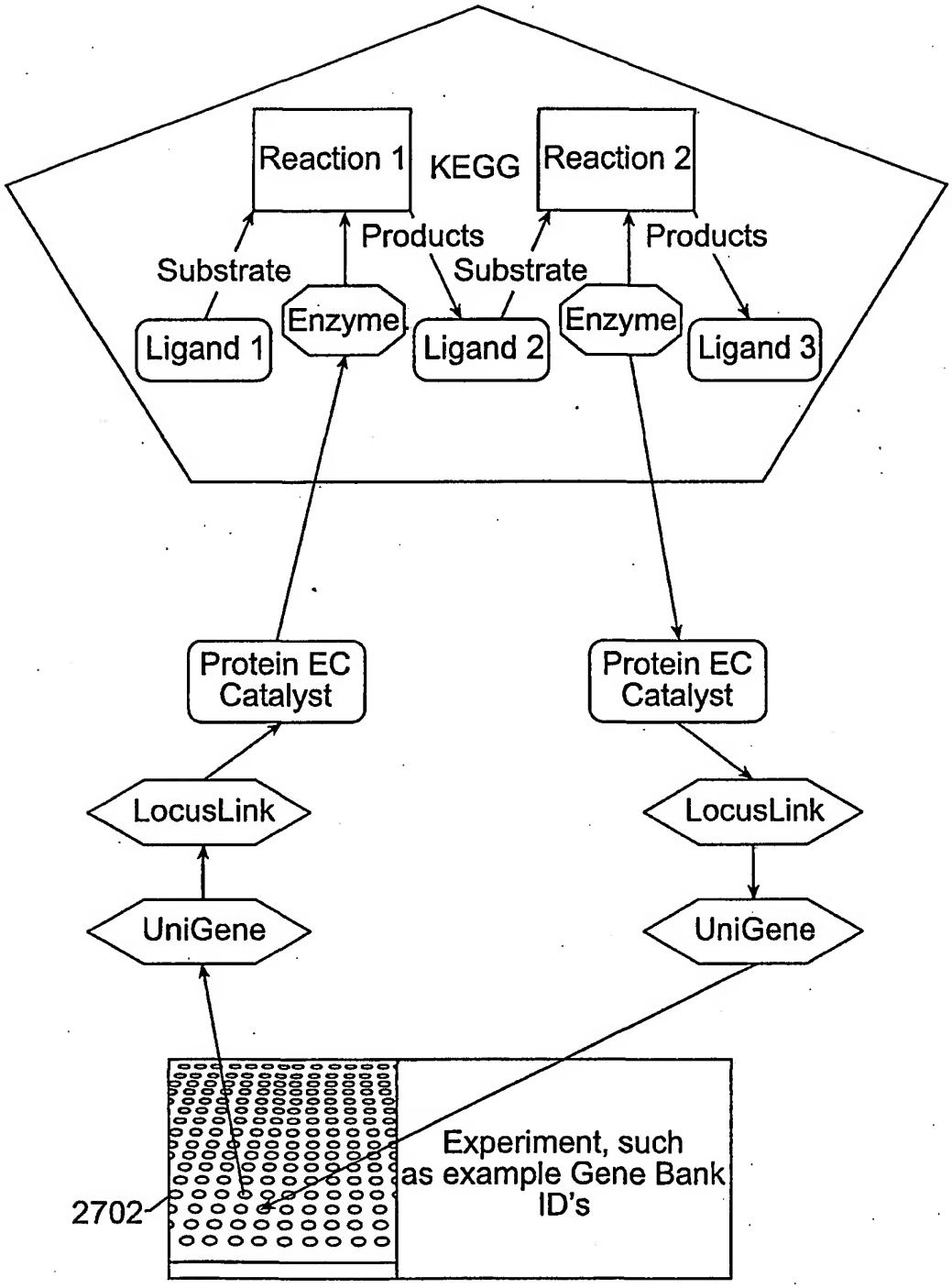

Reaction 1
KEGG
Reaction 2
Products
Products
Substrate
Substrate
Enzyme
Enzyme
Ligand 1
Ligand 2
Ligand 3
Protein EC Catalyst
Protein EC Catalyst
LocusLink
LocusLink
UniGene
UniGene
Experiment, such as example Gene Bank ID's
2702

FIG. 27.

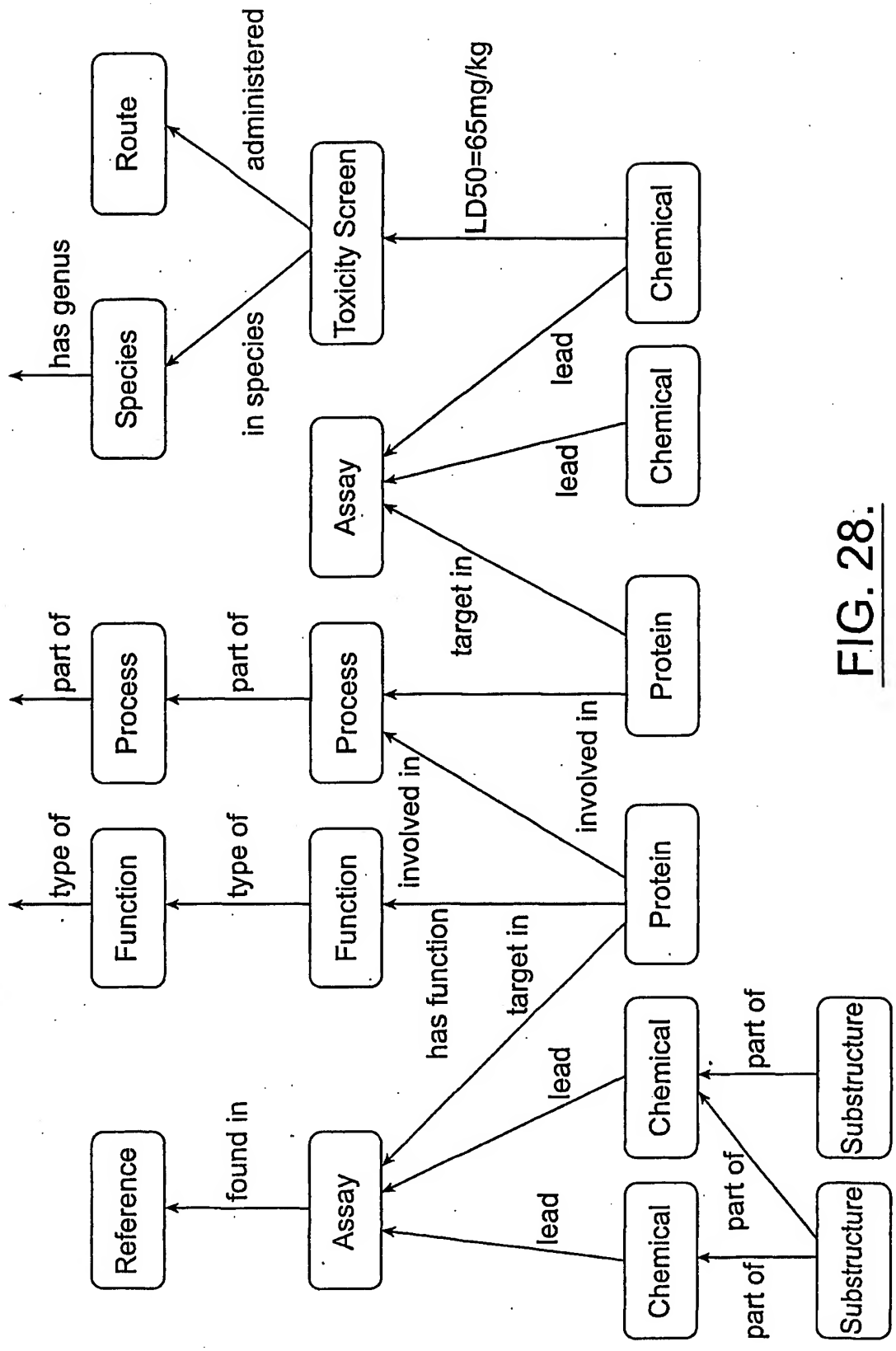

Route
administered
has genus
Species
in species
Toxicity Screen
LD50=65mg/kg
Chemical
Chemical
Chemical
lead
lead
lead
part of
part of
Process
Process
target in
Assay
Protein
type of
type of
involved in
involved in
part of
part of
Function
Function
has function
target in
Protein
Reference
found in
Assay
lead
Chemical
part of
Substructure
part of
Chemical
Substructure

FIG. 28.

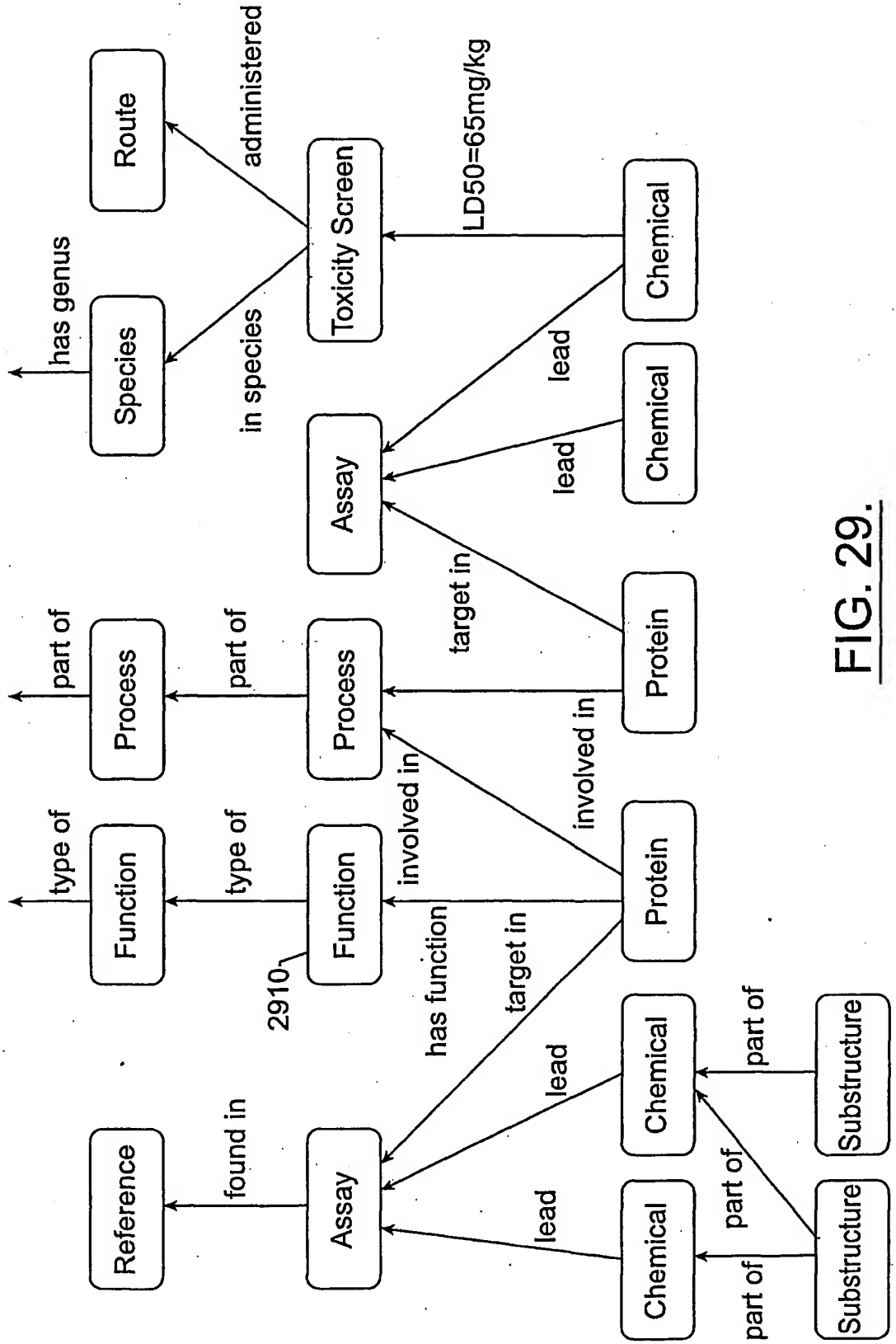

Reference
found in
Assay
lead
Chemical
part of
Substructure
part of
Substructure
part of
Chemical
lead
Chemical
has function
target in
Protein
involved in
Protein
involved in
2910
Function
type of
Function
type of
Function
part of
Process
part of
Process
target in
Assay
lead
Chemical
lead
Chemical
lead
Chemical
LD50=65mg/kg
Toxicity Screen
in species
administered
Species
has genus
Route

FIG. 29.

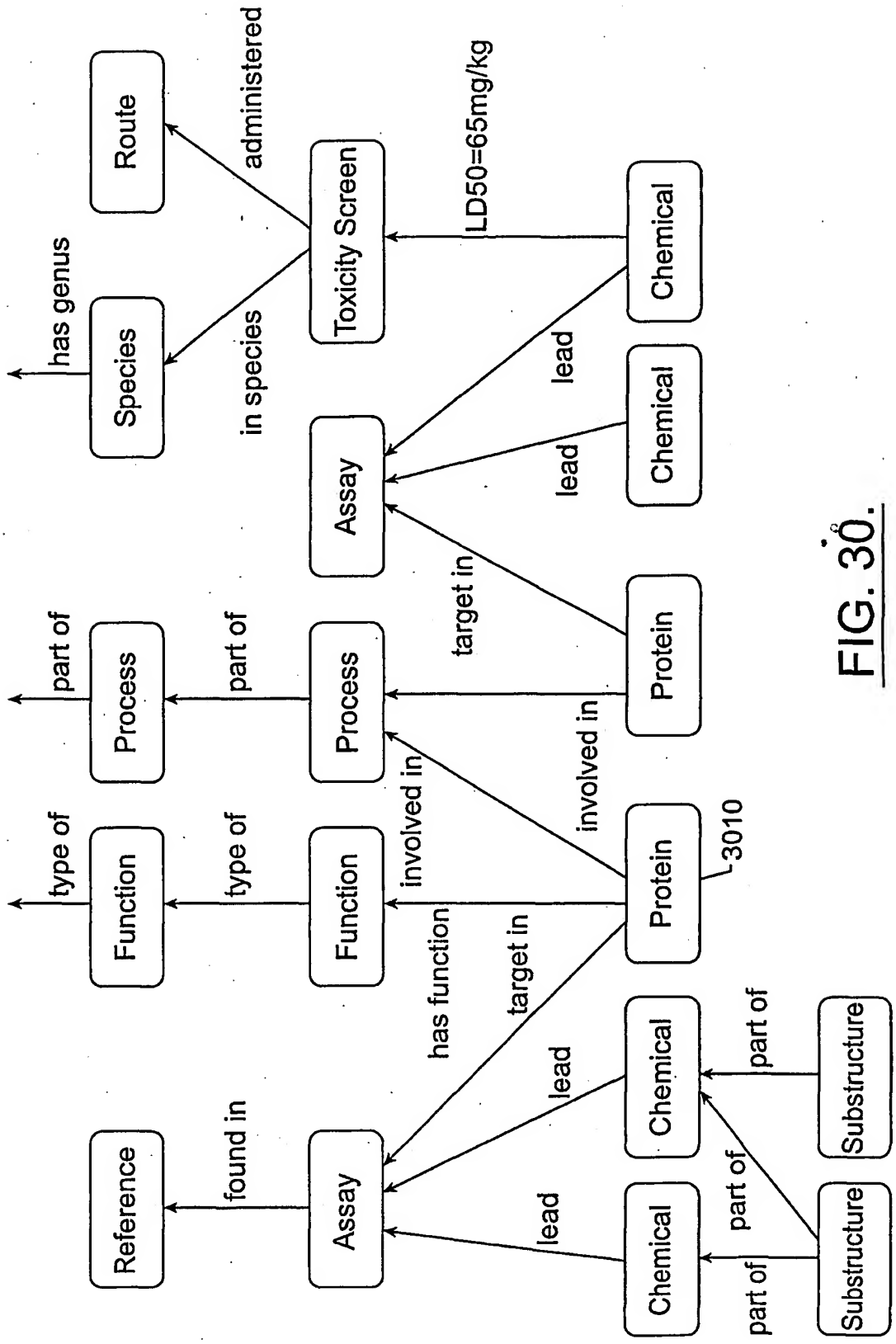

Reference
found in
Assay
lead
Chemical
part of
Substructure
part of
Substructure
lead
Chemical
has function
target in
Protein
3010
involved in
Function
type of
Function
Process
part of
Process
Protein
target in
Assay
lead
Chemical
lead
Chemical
Chemical
LD50=65mg/kg
Toxicity Screen
in species
administered
Species
has genus
Route
part of
Process
type of
Function

FIG. 30.

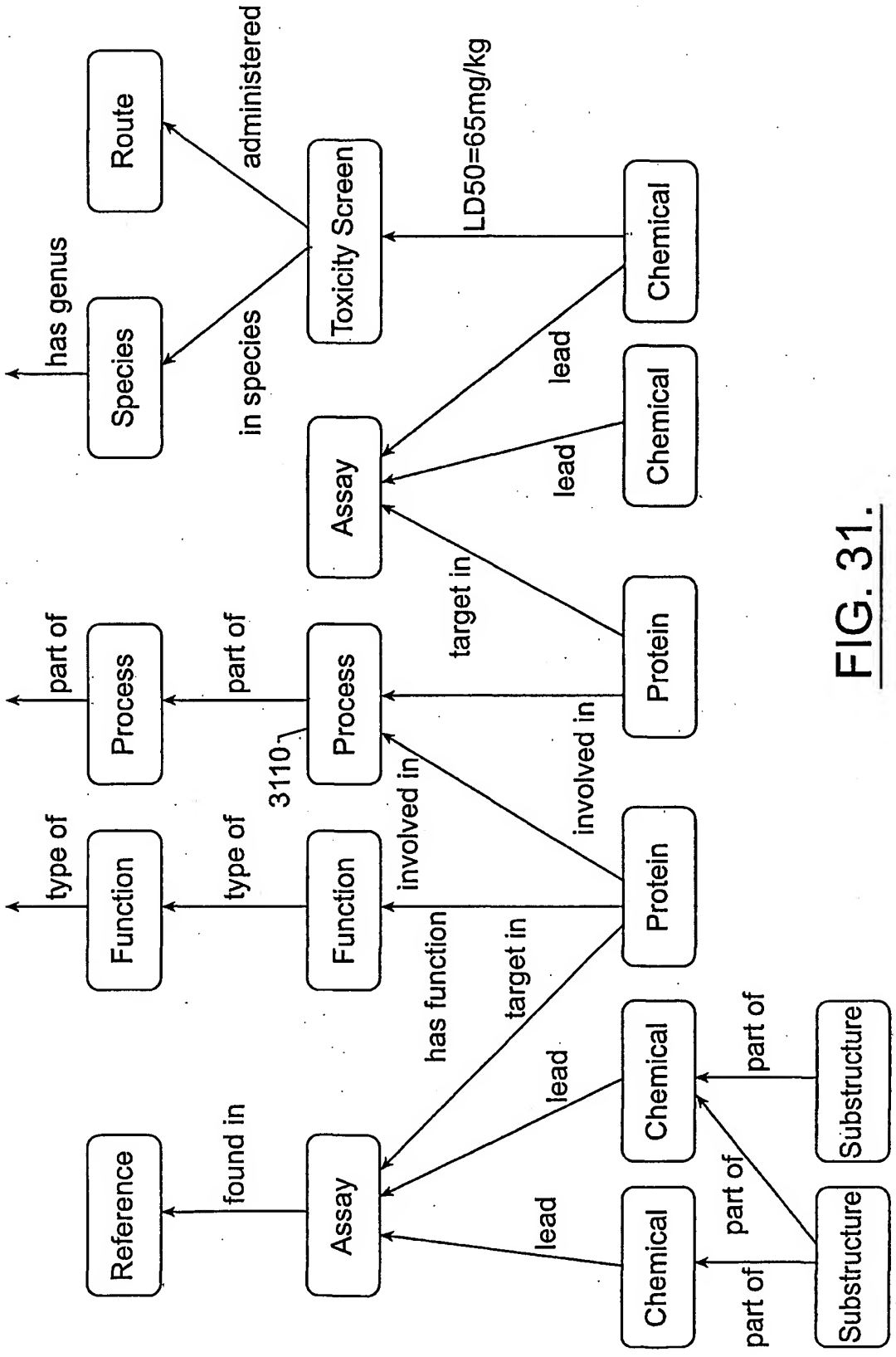

Route
administered
has genus
Species
in species
Toxicity Screen
LD50=65mg/kg
Chemical
part of
Process
part of
Process
Assay
lead
lead
Chemical
Chemical
type of
Function
type of
Function
3110
involved in
target in
Protein
involved in
Protein
has function
target in
Reference
found in
Assay
lead
Chemical
part of
Substructure
lead
part of
Chemical
part of
Substructure

FIG. 31.

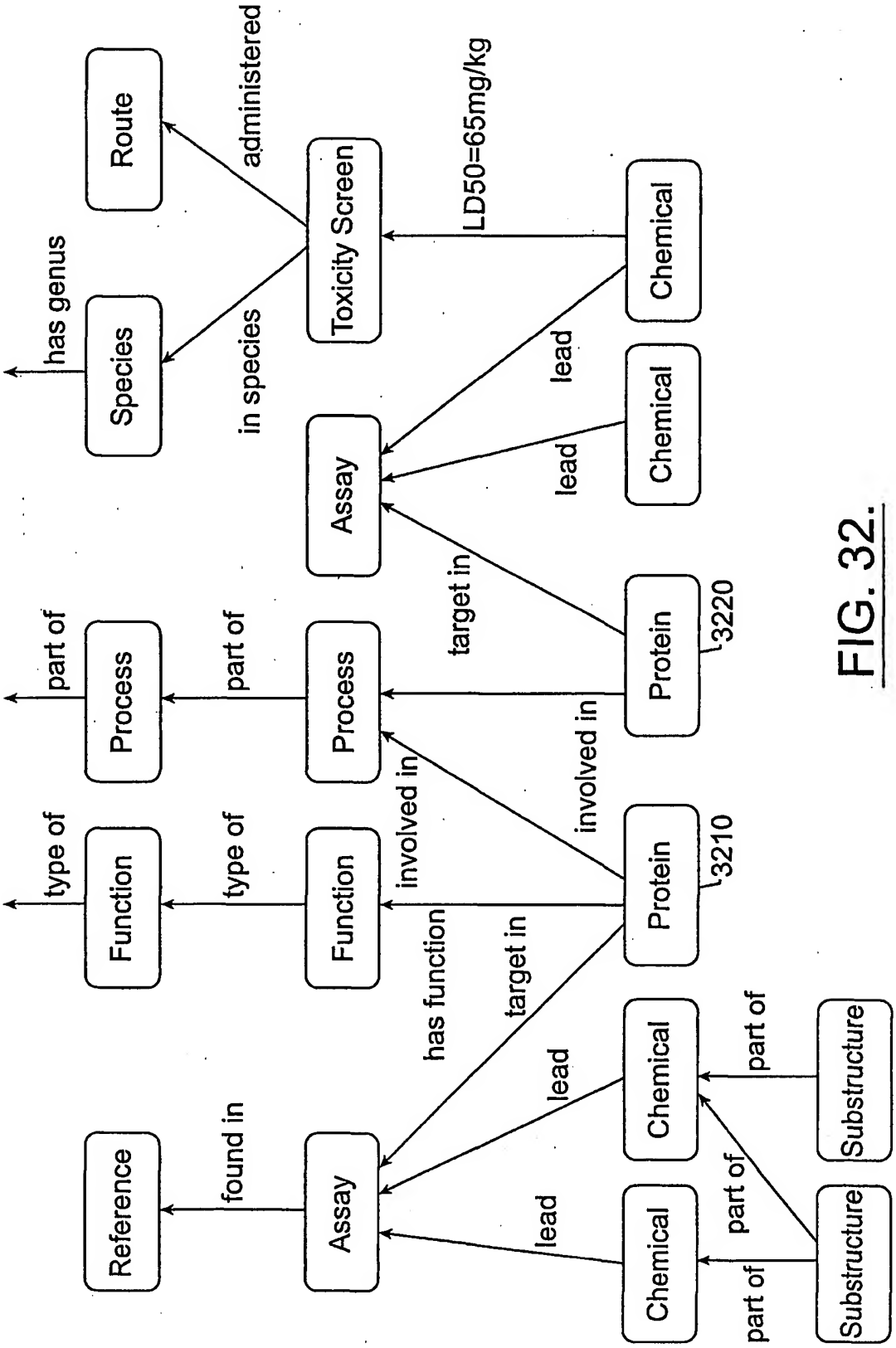

Reference
found in
Assay
lead
Chemical
part of
Substructure
has function
target in
Protein
3210
involved in
Function
type of
Process
part of
target in
Protein
3220
involved in
Function
type of
Process
part of
Assay
lead
Chemical
lead
Chemical
LD50=65mg/kg
Toxicity Screen
in species
administered
Species
has genus
Route

FIG. 32.

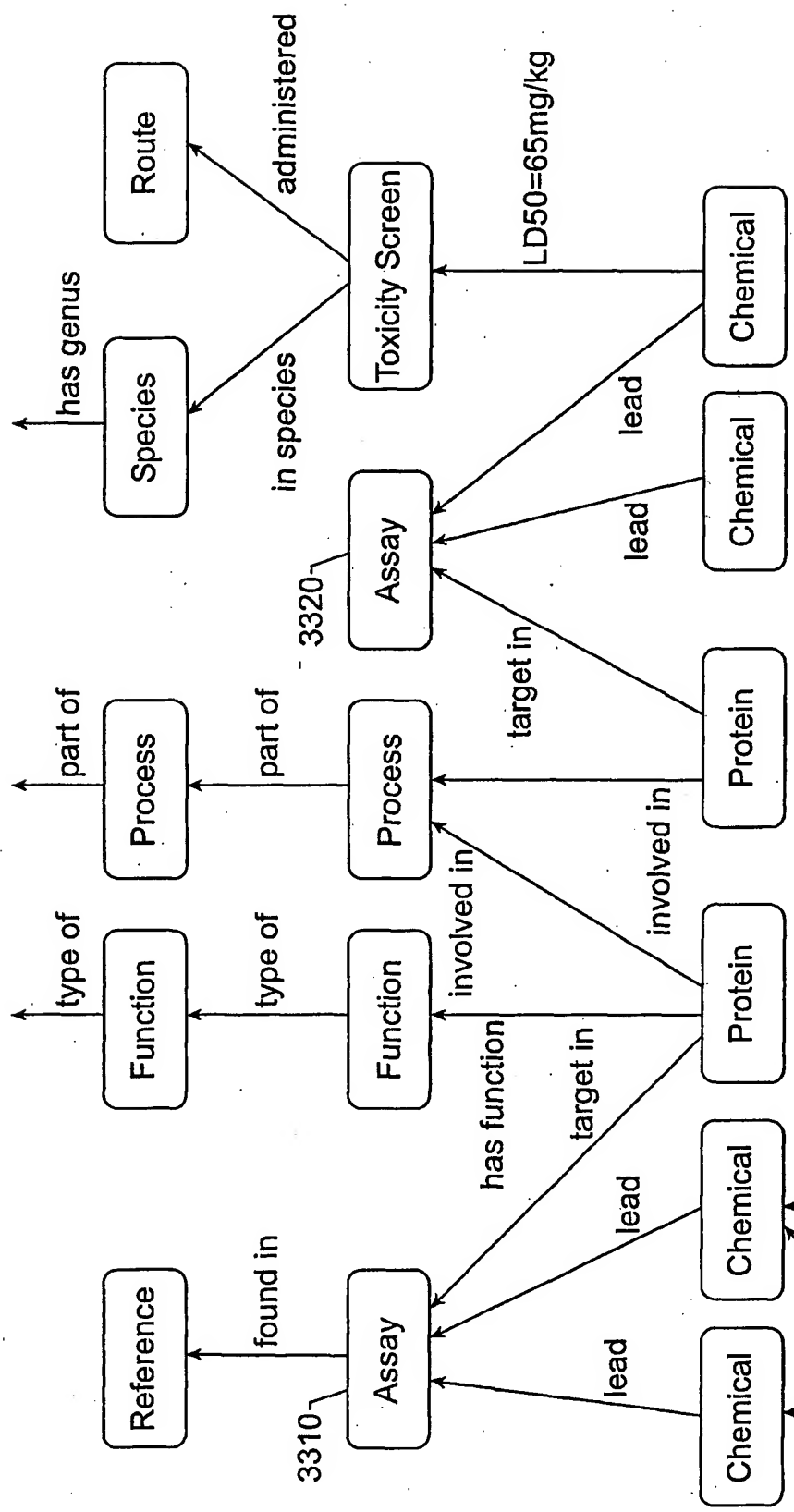

Reference
found in
3310
Assay
Chemical
Chemical
Substructure
Substructure
part of
part of
lead
lead
target in
has function
Function
Function
Protein
Protein
involved in
involved in
type of
type of
Process
Process
part of
part of
target in
type of
Function
Process
part of
3320
Assay
lead
lead
Chemical
Chemical
Chemical
in species
administered
has genus
Species
Route
Toxicity Screen
LD50=65mg/kg

FIG. 33.

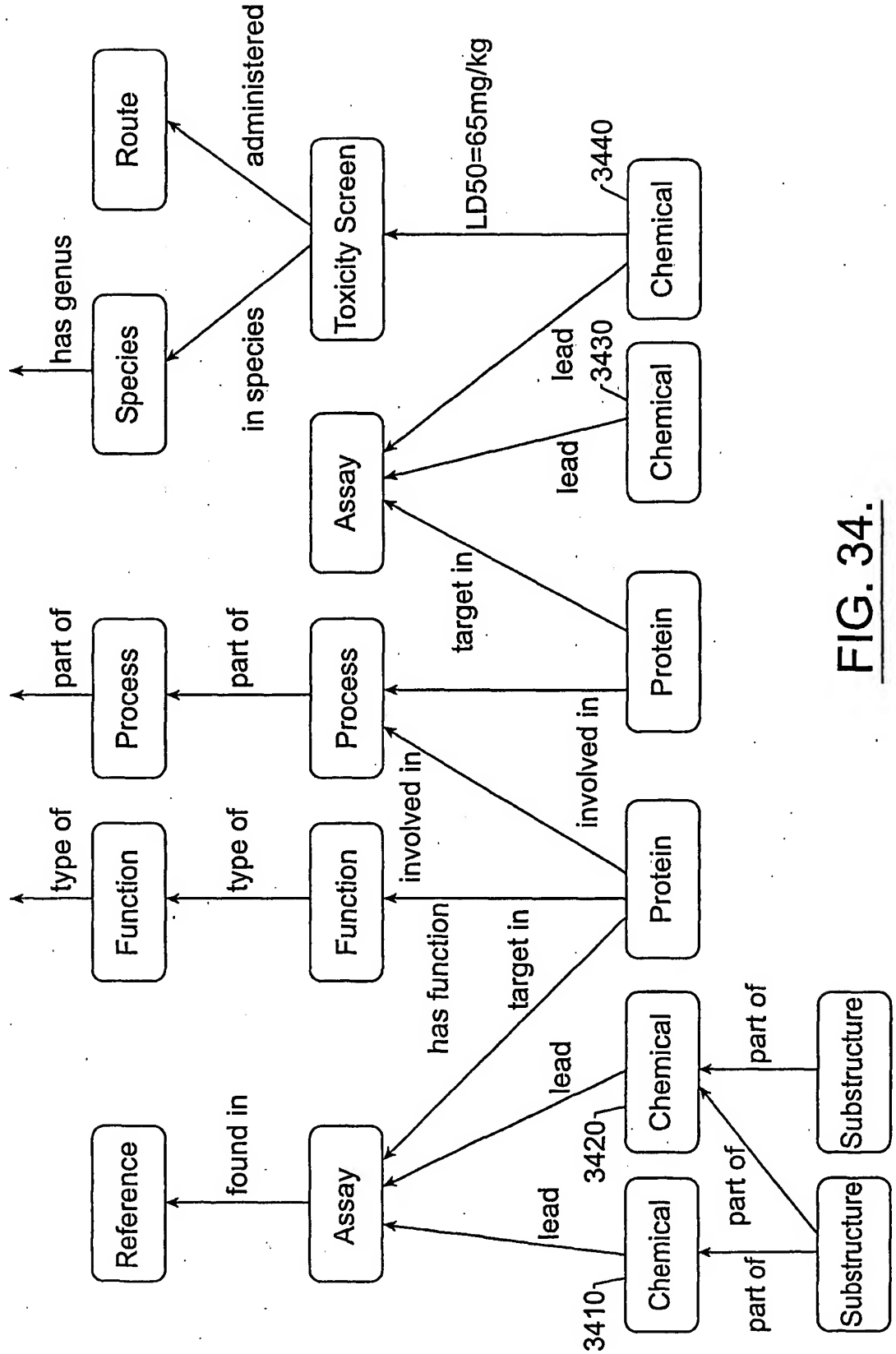

Reference
found in
Assay
lead
3410
Chemical
part of
part of
Substructure
lead
3420
Chemical
part of
Substructure
has function
target in
Protein
involved in
Function
type of
Process
part of
involved in
Function
type of
Process
part of
target in
Protein
Assay
in species
has genus
Species
administered
Route
Toxicity Screen
LD50=65mg/kg
lead
Assay
lead
3430
Chemical
3440
Chemical

FIG. 34.

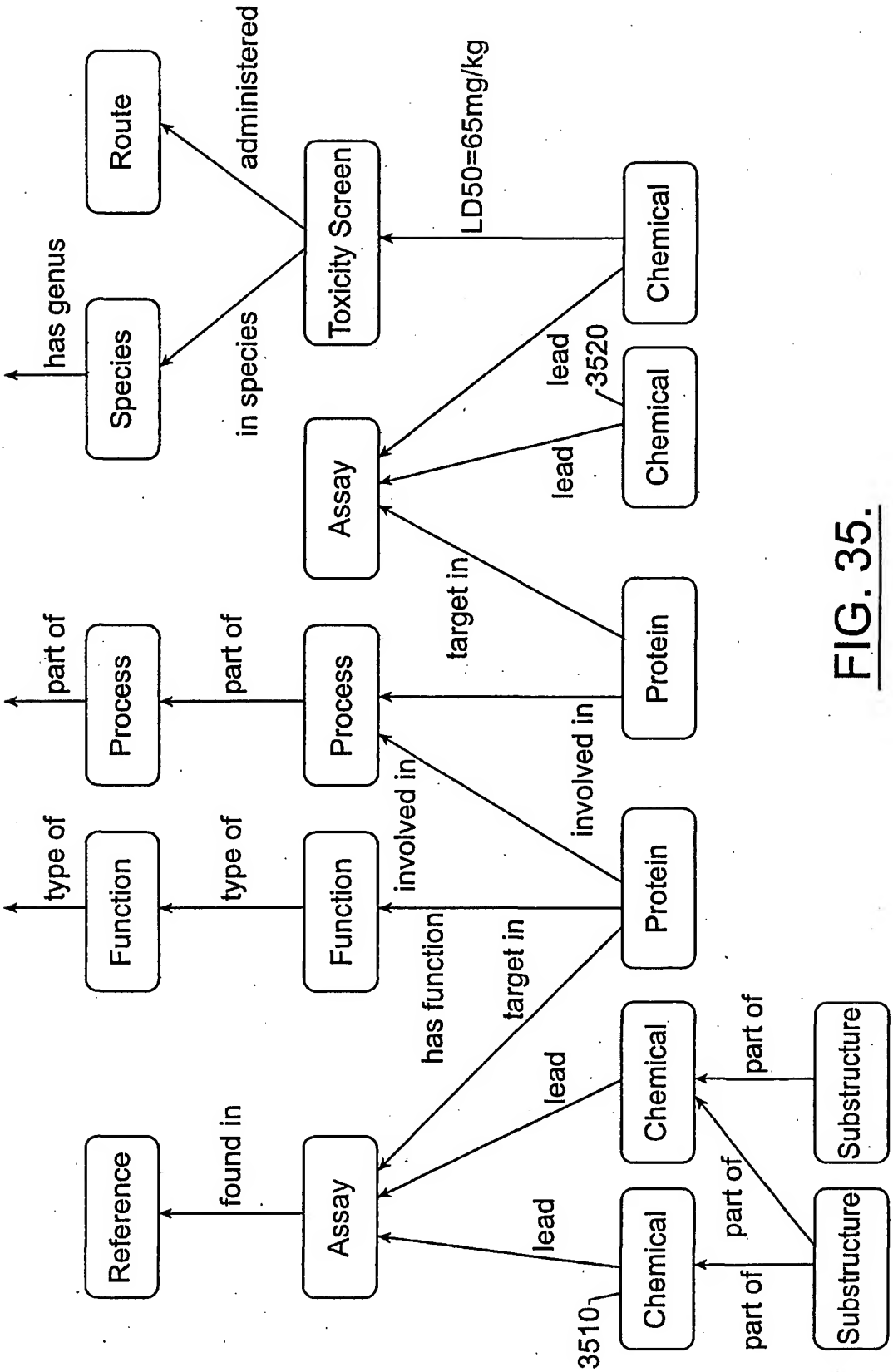

Route
administered
has genus
Species
in species
Toxicity Screen
LD50=65mg/kg
Chemical
lead
3520
Chemical
lead
Assay
target in
Protein
part of
Process
part of
Process
involved in
Protein
type of
Function
type of
Function
involved in
Protein
Reference
found in
Assay
has function
target in
lead
Chemical
part of
Substructure
lead
3510
Chemical
part of
Substructure

FIG. 35.

Incellico
Analytic software for the life sciences

Demonstration of Integrated Ontology Searching

Search for compound screening data

Target

○ SWISS-PROT ID: [ ]

◉ Functional Class: [protein famesyltransferase]

Query Expansion

☑ Expand query by process

☐ Expand query by metabolic pathway

Absorption/Toxicity

☐ LD50 in species: [rat], route: [oral] is more than [100] mg/kg

☐ Show records with no toxicity data.

☐ Qualitative assessment of absorption is [High ▼]

☐ Show records with no absorption data.

Chemical Structure

☐ Must have structural elements: [ ]

☐ Must not have structural elements: [ ]

[Submit Query]

FIG. 36.

PROTEIN FARNESYLTRANSFERASE-1192365509-TABLE 1. IMIDAZOLE-CONTAINING PIPERAZINE INHIBITORS OF FT

Name	CAS-ID	Result
(S)-1-[2-(1H-IMIDAXOL-4-YL)PROPYL]-2-(2-METHOXYETHYL)-4-(1-NAPHTHALENYLCARBONYL)PIPERAZINE	Unknown	IC50=10
(S)-1-(1H-IMIDAZOL-4-YLACETYL)-2-(2-METHOXYETHYL)-4-(1-NAPHTHALENYLCARBONYL)PIPERAZINE, DIHYDROCHLORIDE	Unknown	IC50=34

PROTEIN FARNESYLTRANSFERASE-873874829-TABLE1. INHIBITION CONSTANTS FOR FPP AND GGPP ANALOGUES

Name	CAS-ID	Result
3-VINYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=173
3-TERTIARY-BUTANYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=31
3-ALLYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=189
3-ETHYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=215
3-PHENYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=299
3-VINYL-GERANYLGERANYL-DIPHOSPHATE	Unknown	IC50=715
3-ALLYL-GERANYLGERANYL-DIPHOSPHATE	Unknown	IC50=453

PROTEIN GERANYLGERANYLTRANSFERASE-873874829-TABLE1. INHIBITION CONSTANTS FOR FPP AND GGPP ANALOGUES
Query Expansion: Process–C-TERMINAL PROTEIN PRENYLATION

Name	CAS-ID	Result
3-VINYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=100000
3-TERTIARY-BUTANYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=50000
3-ALLYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=100000
3-ETHYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=100000
3-PHENYL-FARNESYL-DIPHOSPHATE	Unknown	IC50=100000
3-VINYL-GERANYLGERANYL-DIPHOSPHATE	Unknown	IC50=3050
3-ALLYL-GERANYLGERANYL-DIPHOSPHATE	Unknown	IC50=3380

To Fig. 37B.

FIG. 37A.

From Fig. 37A.

PROTEIN GERANYLGERANYLTRANSFERASE-835540405-TABLE 1. ic50 VALUES FOR ENZYME INHIBITION, RAP1A OR H-RAS PROCESSING, AND RELATIVE SELECTIVITY FOR PGGTASE AND PFTASEINHIBITORS 1-20
Query Expansion: Process--C-TERMINAL PROTEIN PRENYLATION

Name	CAS-ID	Result
4-NITRO-2-(1-NAPHTHYL)BENZOATE	Unknown	IC50=44
4-[[N-(1H-IMIDAZOL-2-YL)METHYLENEAMINO]-2-(1-NAPHTHYL)BENZOYL]LEUCINE.	Unknown	IC50=210
4-[[N-(4-PYRIDYL)METHYLENEAMINO]-2-(1-NAPHTHYL)BENZOYLE]LEUCINE.	Unknown	IC50=1600
4-METHOXY-2-PHENYLBENZOATE.	Unknown	IC50=32
4-[[N-(IMIDAZOL-4-YL0METHYLENEAMINO]-2-(1-NAPHTHYL)BENZOYL]LEUCINE.	Unknown	IC50=38
4-[[N-(1-TRITYLIMIDAZOL-4-YL)METHYLENEAMINO]-2-PHENYLBENZOYL]LEUCINE METHYL ESTER.	Unknown	IC50=90

FIG. 37B.

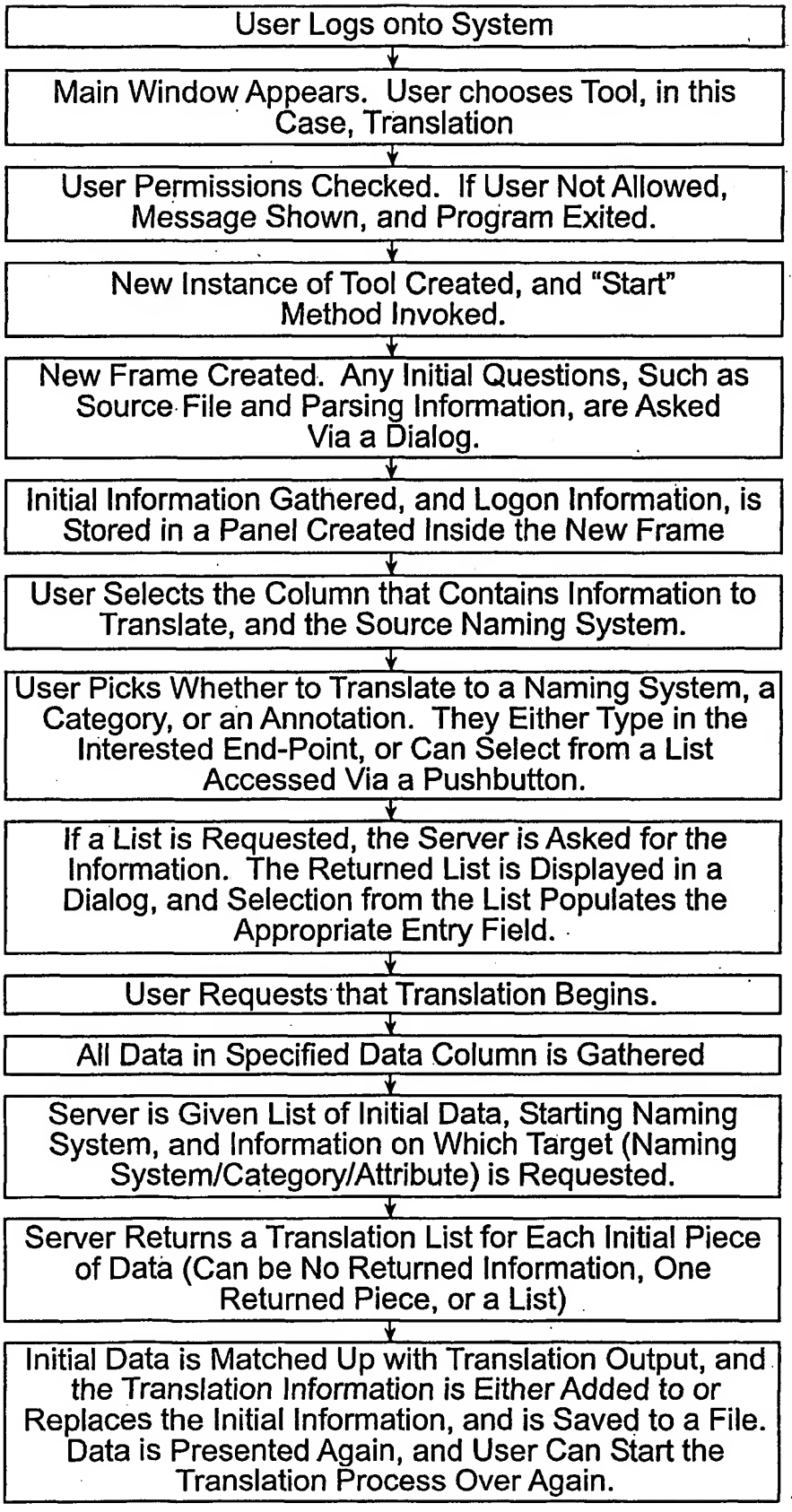

User Logs onto System
Main Window Appears. User chooses Tool, in this Case, Translation
User Permissions Checked. If User Not Allowed, Message Shown, and Program Exited.
New Instance of Tool Created, and "Start" Method Invoked.
New Frame Created. Any Initial Questions, Such as Source File and Parsing Information, are Asked Via a Dialog.
Initial Information Gathered, and Logon Information, is Stored in a Panel Created Inside the New Frame
User Selects the Column that Contains Information to Translate, and the Source Naming System.
User Picks Whether to Translate to a Naming System, a Category, or an Annotation. They Either Type in the Interested End-Point, or Can Select from a List Accessed Via a Pushbutton.
If a List is Requested, the Server is Asked for the Information. The Returned List is Displayed in a Dialog, and Selection from the List Populates the Appropriate Entry Field.
User Requests that Translation Begins.
All Data in Specified Data Column is Gathered
Server is Given List of Initial Data, Starting Naming System, and Information on Which Target (Naming System/Category/Attribute) is Requested.
Server Returns a Translation List for Each Initial Piece of Data (Can be No Returned Information, One Returned Piece, or a List)
Initial Data is Matched Up with Translation Output, and the Translation Information is Either Added to or Replaces the Initial Information, and is Saved to a File. Data is Presented Again, and User Can Start the Translation Process Over Again.

FIG. 38.

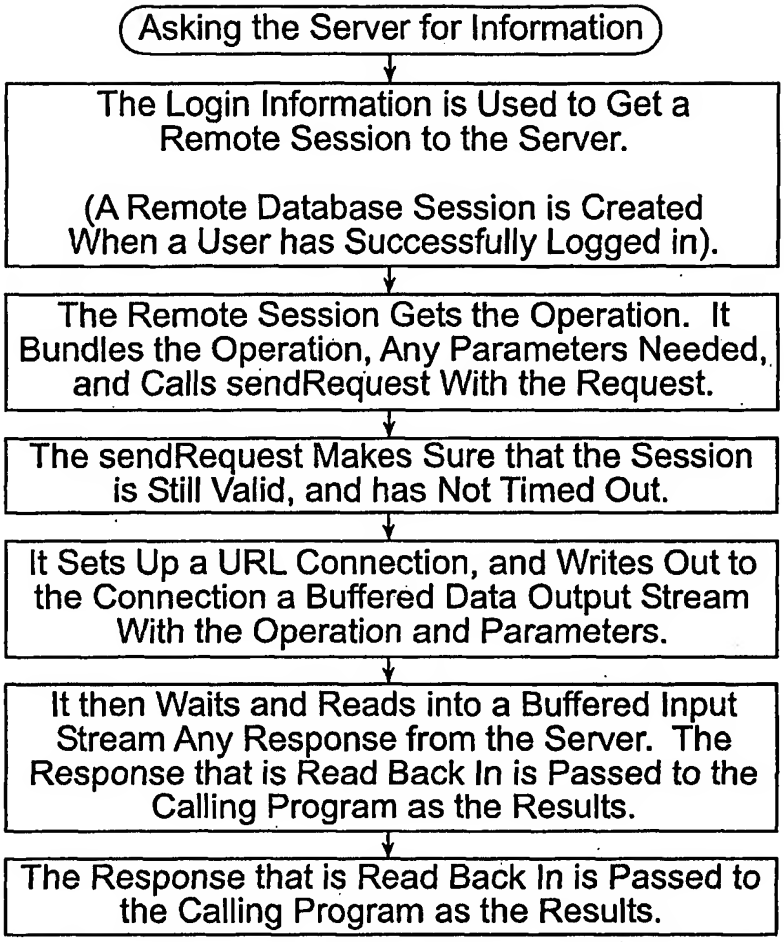

Asking the Server for Information
The Login Information is Used to Get a Remote Session to the Server.
(A Remote Database Session is Created When a User has Successfully Logged in).
The Remote Session Gets the Operation. It Bundles the Operation, Any Parameters Needed, and Calls sendRequest With the Request.
The sendRequest Makes Sure that the Session is Still Valid, and has Not Timed Out.
It Sets Up a URL Connection, and Writes Out to the Connection a Buffered Data Output Stream With the Operation and Parameters.
It then Waits and Reads into a Buffered Input Stream Any Response from the Server. The Response that is Read Back In is Passed to the Calling Program as the Results.
The Response that is Read Back In is Passed to the Calling Program as the Results.

FIG. 39.

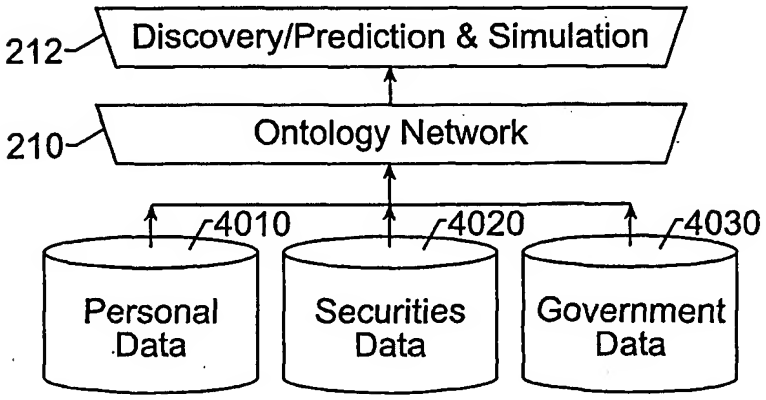

212
Discovery/Prediction & Simulation
210
Ontology Network
4010
4020
4030
Personal Data
Securities Data
Government Data

FIG. 40.

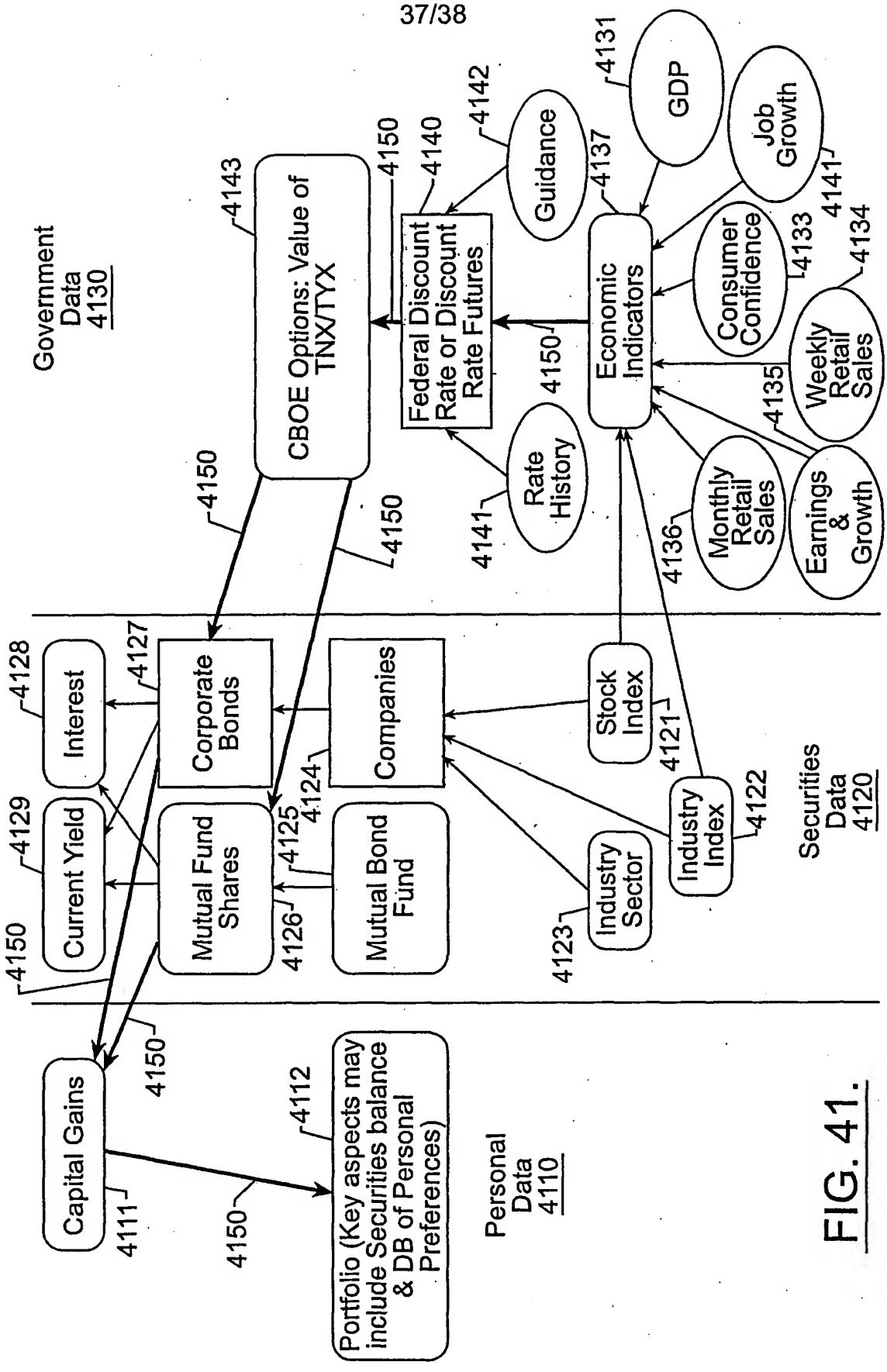

Government Data 4130
CBOE Options: Value of TNX/TYX
4143
4150
4140
Federal Discount Rate or Discount Rate Futures
4142
Guidance
4131
GDP
Job Growth
4141
Economic Indicators
4137
Consumer Confidence
4133
Weekly Retail Sales
4134
4135
Earnings & Growth
Monthly Retail Sales
4136
Rate History
4141
4150
Securities Data 4120
Corporate Bonds
4127
Interest
4128
Current Yield
4129
Mutual Fund Shares
4125
Mutual Bond Fund
4126
Companies
4124
Stock Index
4121
Industry Index
4122
Industry Sector
4123
Personal Data 4110
Capital Gains
4111
Portfolio (Key aspects may include Securities balance & DB of Personal Preferences)
4112

FIG. 41.

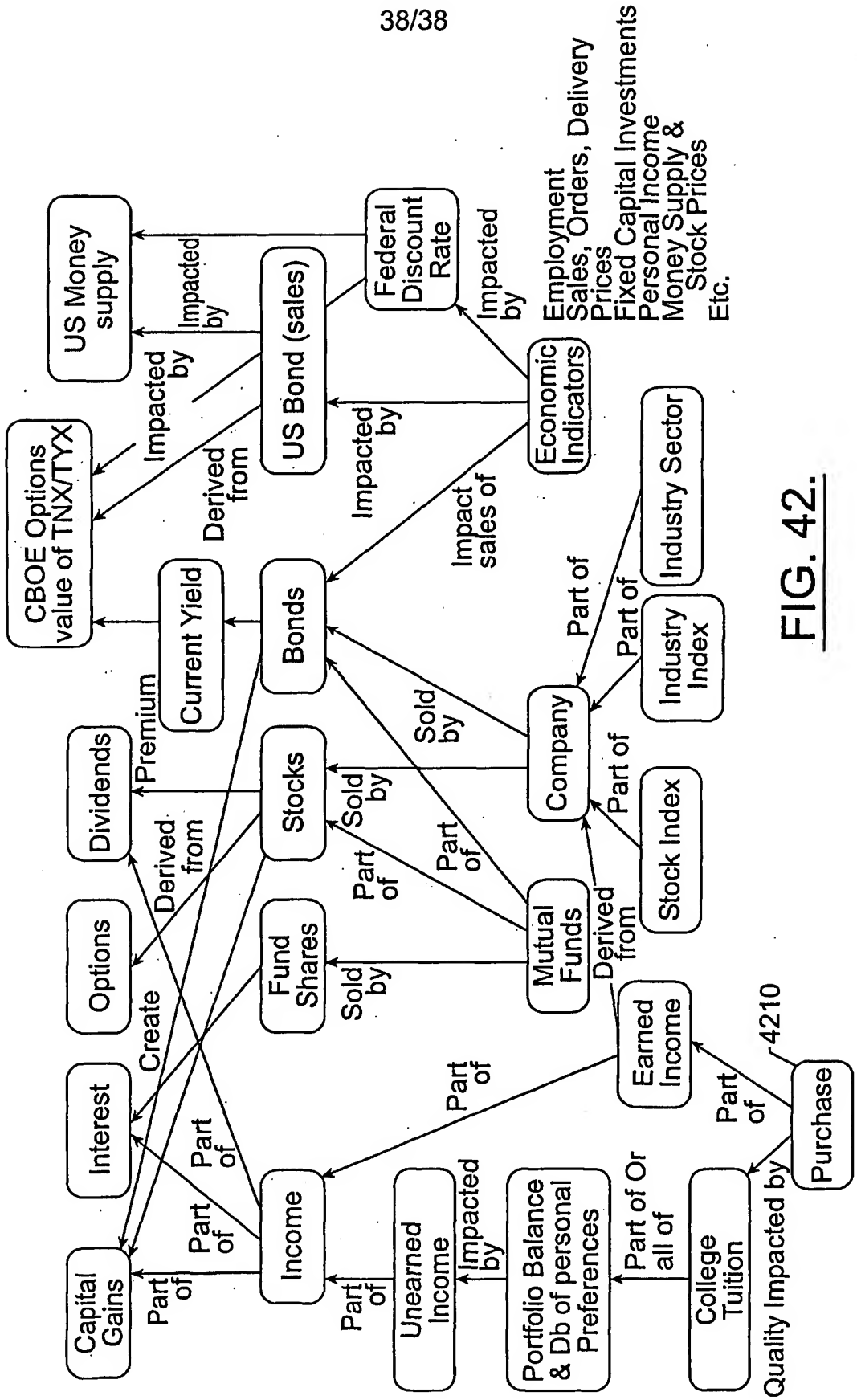

Capital Gains
Part of
Income
Part of
Interest
Create
Options
Derived from
Dividends
Premium
Current Yield
CBOE Options value of TNX/TYX
Impacted by
US Money supply
Impacted by
Derived from
US Bond (sales)
Impacted by
Federal Discount Rate
Impacted by
Economic Indicators
Employment
Sales, Orders, Delivery
Prices
Fixed Capital Investments
Personal Income
Money Supply &
Stock Prices
Etc.
Impact sales of
Bonds
Part of
Stocks
Sold by
Fund Shares
Sold by
Sold by
Company
Part of
Industry Sector
Part of
Industry Index
Part of
Mutual Funds
Derived from
Stock Index
Part of
Earned Income
Part of
Unearned Income
Impacted by
Portfolio Balance & Db of personal Preferences
Part of Or all of
College Tuition
Quality Impacted by
Part of
4210
Purchase

FIG. 42.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/16406

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : G06F 19/00
US CL : 702/19
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 702/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	XU et al. Some Experience Using OODB in the Interoperation of Heterogeneous Genome Database Systems. Proceedings of the 1996 Engineering Systems Design and Analysis Conference. July 1996, Vol. 2, pages 53-61, especially page 56.	1-115
Y	US 5,859,972 A (SUBRAMANIAM ET AL) 12 January 1999 (12.01.1999), columns 1-3.	1-115

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
13 July 2002 (13.07.2002)

Date of mailing of the international search report
27 AUG 2002

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703)305-3230

Authorized officer
John S. Brusca Felicia D. Roberts for
Telephone No. 703 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/16406

Continuation of B. FIELDS SEARCHED Item 3:
U.S. Patent, Derwent World Patent Index
search terms: search, database, link, integrate, biological, chemical

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/16406

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claim Nos.: 116 and 117
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 116 and 117 were not searched because they are drawn to mere representation of information which is excluded from searching under PCT Rule 39.

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.